SCIENCE

13 March 1959

Volume 129, Number 335

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Your scientists and engineers now benefit from electronic computation without becoming computer specialists!

How to get increased research and engineering productivity without increased manpower

Electronic computation in the right hands. The lowest-priced complete computer you can buy, the Royal Precision LGP-30 enables both present and new computer users to bring electronic computation *to a level where it does the most good.* No longer do you need a group of highly-specialized computer men. The compact, mobile LGP-30 plugs into any convenient wall outlet without expensive installation or air-conditioning . . . puts electronic computation *in the hands of your own research and engineering specialists* . . . greatly increases their available creative time and productive output.

Short break-in time; fast answers. Although the LGP-30 gives you memory (4096 words) and capacity comparable to that of computers many times its size and cost, it is by far the easiest computer to learn and program. Answers are printed out directly – require no deciphering. Result: because the people qualified in your specific field are given access to the computer, you get an almost immediate increase in productivity. At one LGP-30 installation, for instance, an output of 34 engineers has been attributed to a staff of only four.

Elimination of tedium; increased quality. A survey of your research and engineering work would undoubtedly show much of it to be of a routine nature –the repetitive calculations known to be deadly to the morale of highly-trained personnel. In fact, one research organization estimates that creative thinking and routine calculation are usually found in the ratio of 1 to 9. Using the LGP-30, your engineers can eliminate the tedious 9 parts out of 10 . . . can not only increase output per man but, equally important, improve the quality of the work produced.

Maximum results; minimum cost. Successfully employed in well over 200 installations, the LGP-30 is available on either a sale or rental basis . . . gives you the opportunity to investigate electronic computation without the attendant burdens of high cost and complexity. Backed by 20 years of electronics experience, LGP-30 sales and service are available through Royal McBee offices coast-to-coast. Training is free—as well as membership in an active users organization. A complete library of programs and sub-routines is available.

Write today for complimentary brochure. To discover more fully how the LGP-30 can serve your engineers and your organization, call your nearby Royal McBee Data Processing Representative, or write Royal McBee Corporation, Data Processing Division, Port Chester, N. Y. for illustrated brochure. In Canada: 179 Bartley Drive, Toronto 16.

ROYAL McBEE • *data processing division*

SCIENCE is published weekly by the AAAS, 1515 Massachusetts Ave., N.W, Washington 5, D.C. Entered at the Lancaster, Pa., Post Office as second class matter under the act of 3 March 1879. Annual subscriptions: $8.50; foreign postage, $1.50; Canadian postage, 75¢.

Letters

Vertebrate Metamorphosis

Biological teaching in its manifold aspects emphasizes cyclical development in nature. In his article George Wald gives interesting details, supported by chemical evidence, of two opposed metamorphoses in fishes, one bringing a fish to maturity, the second one returning it to its natal environment [*Science* **128**, 1481 (1958)]. He admits that in land vertebrates physiological changes of the second type do not take place but contends that the entry of a single representative cell, the spermatozoon, into the womb is an analogous event, leading to the completion of the life cycle of such animals in water.

This appears to be open to question. What I find far more objectionable, however, is his use of a Biblical quotation, which is cut short, obviously to lend support to his thesis. To Nicodemus' question as to how a man could be reborn, "can he enter the second time into his mother's womb, and be born? Jesus answered, Verily, verily, I say unto thee, Except a man be born of water . . ." (this is where Wald leaves off). However, the sentence continues: ". . . and of the Spirit, he cannot enter into the kingdom of God." Nobody who knows anything at all about Christian teaching would believe that Jesus is talking about physical rebirth. He is solely concerned with spiritual conversion.

To prevent misrepresentation of this kind in the future, I believe it would be wise for the editors of *Science* to check carefully on authors' use of references from fields other than their own.

PAUL H. KOPPER
Biology Department, Washburn University, Topeka, Kansas

Quantitative Gram Reaction

The semiquantitative evaluation of the Gram reaction reported by T. Mittwer (*1*) is based on applying small amounts of stained and iodinated suspensions of bacterial cells as spots to filter paper, as in paper chromatographic techniques. The resulting streaks of crystal violet are compared for length, as it is assumed that variation in length depends upon the degree of Gram staining behavior, the most Gram-positive species showing the longest streak.

In principle Mittwer's method appears to be a suitable one. However, his staining of bacteria with an overdiluted crystal violet solution (0.1 percent) reduces the relevance and reliability of his evaluation of the degree of Gram-positive behavior. This is especially so since, as Barbaro and Kennedy have conclusively demonstrated, an increase in dye concentration is accompanied by a *differential* dye uptake between Gram-positive and Gram-negative bacteria (*2*). These authors used 10-percent solutions of crystal violet in accordance with the recommended range (1 to 10 percent) of the Gram staining procedure (*2*). My model experiments also illustrate the fact that uptake of crystal violet by proteins can be substantially increased by raising the concentration of the dye. For example, in 10 minutes 1 mg of casein and 1 mg of iodinated casein take up 1.7 and 2.6 μg, respectively, of crystal violet from a Tris-buffered (*p*H 7.2) $10^{-5}M$ dye solution at 20°C; a sixfold increase in dye concentration raises the previous values to 4.2 and 7.2 μg, respectively. The data were obtained with the aid of a Perkin-Elmer Spectracord spectrophotometer at $H_2O = 595$ mμ. If, however, we deal with bacteria rather than proteins, a suboptimal range of 0.1-percent in dye concentration must be considered. In and below that critical range the differential in crystal violet uptake between a Gram-positive and a Gram-negative organism ceases to exist (*3*).

Finally, it should be pointed out that a semimicro method for measuring the degree of Gram-positive staining behavior of bacteria and other biological material has been published (*4*). We used a concentration of 1-percent crystal violet and a chromatographic technique, separating the total amount of dye taken up by bacteria into compact spots; then the spots were eluted, and their dye content was quantitatively determined with a spectrophotometer.

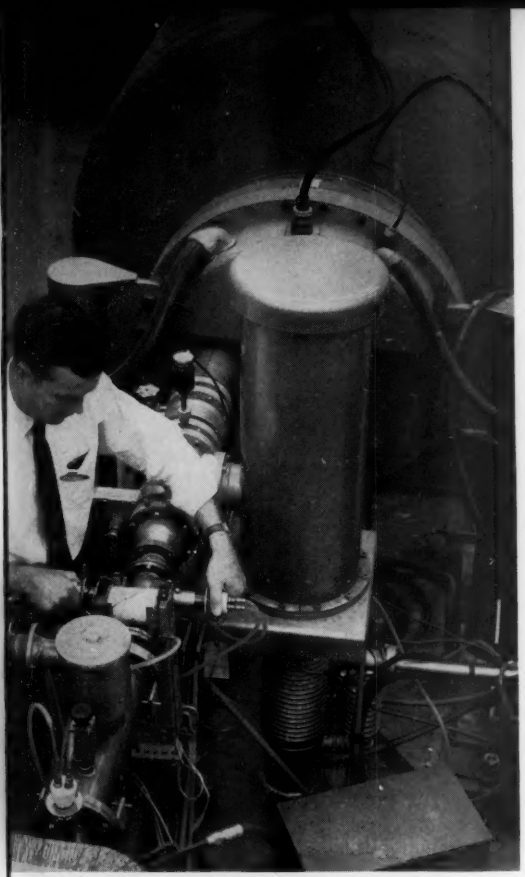
ROLAND FISCHER
Ohio State University Health Center, Columbus Psychiatric Institute and Hospital, Columbus

References

1. T. Mittwer, *Science* 128, 1213 (1958).
2. J. F. Barbaro and E. R. Kennedy, *J. Bacteriol.* 67, 603 (1954).
3. F. Wensinck and J. Boevé, *J. Gen. Microbiol.* 17, 401 (1957).
4. Society of American Bacteriologists, *Manual of Methods for Pure Culture Study of Bacteria* (Geneva, N.Y., 1946), vol. 4, pp. 51–58; R. Fischer, *Naturwissenschaften* 45, 287 (1958).

Roland Fischer's comment appears to be based upon my use of an "overdiluted" solution of crystal violet. It is true that an increase in dye concentration can be correlated with an increase in "dye uptake" by a constant amount of bacterial cell material, with the time of contact constant (*1*). However, no reduction in the reliability of my method should result from the use of 0.1-percent dye solution, since numerous tests have established the validity of this concentration in routine qualitative Gram differentiation. Such tests can be confirmed by anyone in a few minutes. In fact, a rather

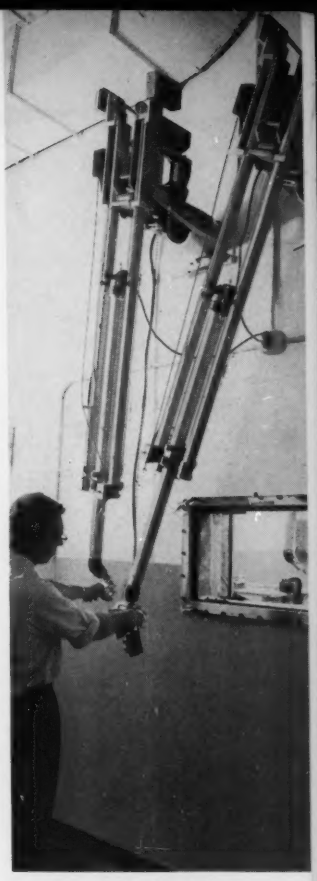
(*Continued on page 730*)



3 mev Van de Graaff accelerator – typical of advanced equipment used by Lockheed research scientists.

PHYSICS

Expanding the Frontiers of Space Technology



"Hot cell," for advanced radiation research in the nuclear physics laboratory.

Lockheed Missiles and Space Division is engaged in a broad, long-range program of basic scientific research at its Research and Development Laboratories in the Stanford Industrial Park at Palo Alto, California. Its modern facilities include a 3.5 mev Van de Graaff accelerator; a variety of shock tubes; extensive equipment for plasma and spectroscopic research; and one of the most modern computing centers in the nation. The Division was honored at the first National Missile Industry Conference as "the organization that contributed most during the past year to the development of the art of missiles and astronautics" and has several of the country's major programs under development.

A group of over fifty physicists is presently engaged in research and the fundamental investigation of problems in the following areas:

Nuclear Physics: Including the measurement and theory of nuclear cross sections; B-ray spectroscopy; theory of nuclear structure; reactor physics.

Weapon System Physics: The phenomenology and effects of atomic weapons, including laboratory simulation of radiation.

Space Physics: The study of the earth's upper atmosphere and beyond, including solar-terrestrial interactions.

Plasma Physics: The theoretical and experimental study of transport properties; micro-wave diagnostics; and magneto-hydrodynamics.

Atomic Physics: Mass spectroscopy; theory and measurements of low energy interactions.

Members of the technical staff have every opportunity to participate in the initiation of advanced technological developments. The company encourages and sponsors individual communication with other scientists, the publication of papers and articles, and participation in symposiums and conventions.

If you have an advanced degree in physics, you are invited to join us in one of the most interesting basic scientific research programs in the nation. Write: Research and Development Staff, Dept. C-44, 962 W. El Camino Real, Sunnyvale, Calif.

"The organization that contributed most in the past year to the advancement of the art of missiles and astronautics." NATIONAL MISSILE INDUSTRY CONFERENCE AWARD

Lockheed / **MISSILES AND SPACE DIVISION** / SUNNYVALE, PALO ALTO, VAN NUYS, SANTA CRUZ, SANTA MARIA, CALIFORNIA CAPE CANAVERAL, FLORIDA ALAMOGORDO, NEW MEXICO

Research and Development facilities in the Stanford Industrial Park at Palo Alto where much of the work in physics is conducted.

13 March 1959, Volume 129, Number 3350

SCIENCE

SCIENCE, which is now combined with THE SCIENTIFIC MONTHLY, is published each Friday by the American Association for the Advancement of Science at Business Press, Lancaster, Pa. The joint journal is published in the SCIENCE format. Entered at the Lancaster, Pa., Post Office as second class matter under the Act of 3 March 1879. SCIENCE is indexed in the *Reader's Guide to Periodical Literature*.

Editorial and personnel-placement correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. For detailed suggestions on the preparation of manuscripts, book reviews, and illustrations, see *Science* 125, 16 (4 Jan. 1957).

Display-advertising correspondence should be addressed to SCIENCE, Room 740, 11 West 42 St., New York 36, N.Y.

Change of address notification should be sent to 1515 Massachusetts Ave., NW, Washington 5, D.C., 4 weeks in advance. If possible, furnish an address stencil label from a recent issue. Be sure to give both old and new addresses, including zone numbers, if any.

Annual subscriptions: $8.50; foreign postage, $1.50; Canadian postage, 75¢. Single copies, 35¢. Cable address: Advancesci, Washington.

Science and Art

The *Bulletin of the Atomic Scientists* drops its customary business in the February issue to search for common ground between science and art. Essays by scientists, artists, and critics examine some of the misconceptions that scientists entertain about art, and that artists entertain about science. Although the problems raised in the exchange are not altogether new, they are worth a fresh airing. With science flourishing as never before, we are glad to report that a journal, usually devoted to science and its implications, stops to consider how the other half lives.

In one essay, H. W. Janson, professor of fine arts at New York University, undertakes to answer a common criticism of modern art, a criticism, moreover, that recently took on some scientific authority. Facing an example of Abstract Expressionism in a gallery, the museum-goer insists that a child or an ape could paint a picture as good as that. Scientific support for this contention comes from the Baltimore Zoo. Several years ago, Betsy, an obliging chimpanzee, produced some paintings that even art critics found practically indistinguishable from examples of nonrepresentational art.

By way of answer to Betsy and her champions, Janson suspects that if the chimp's paintings have esthetic merit, the keeper, not Betsy, deserves the credit. True, Betsy applied the paint to the canvas, and probably to other nearby objects as well, but the keeper remained at her elbow. When she produced a pattern that seemed to be a passable abstraction, he simply relieved her of the canvas. If the keeper had been interested in a portrait of himself, he might have had to wait a long time, but even in the task of matching nonrepresentational art, the keeper had to wait for what was essentially a source of random patterns to produce what he had in mind.

In another essay, Marston Morse, professor of mathematics at the Institute for Advanced Study in Princeton, examines the claim that science and art are as different in their concerns as mind and heart. If products of these two enterprises are different, the claim runs, then so must be the qualities that go into their making.

As part of his answer to this claim, Morse argues that esthetic judgment plays an important role in the construction of scientific theories, and he offers some examples from recent work in mathematics and physics. He finds that the mathematical representation of observation and experiment is not uniquely determined by observation and experiment. Scientists have a choice among a multiplicity of mathematical forms, and the forms they select depend significantly upon intuitions of simplicity and balance. Perhaps that is why scientists, as well as artists, are unable to explain the causes of their inspiration.

All told, the special issue of the *Bulletin* contains ten essays. Collectively, they serve to develop some of the qualities and values that science and art share. But the search for common ground does strike an ironic note. The irony is that science may now be enjoying greater public esteem than art because of properties that it alone possesses. Public support of research continues to grow not because people are learning that science begins in wonder, but because they are learning that science can end in dollars. Possibly the general attitude is: I may not know anything about science, but I do know what I like.—J.T.

OVER 10,000 IN DAILY USE . . .
JOB-RATED *EXCELLENT FOR**

W-I-D-E TEST RANGE

* "Excellent for analyzing fuel oil, slags, boiler water, metals, flue gas, etc. We're recommending its use in the labs of our power plants."
Leading Power & Light Co.
—name on request.

BAUSCH & LOMB
Spectronic 20
COLORIMETER

This low-cost "production tool" gives you quick, dependable photometric readings . . . easy as tuning your radio! In many industries it's basic equipment for quality control testing, inspection . . . even research! Here's why:

- **DEPENDABLE ACCURACY!** Narrow band pass (only 20mμ!) assures highest spectral purity.
- **EASIEST TO USE!** Dial instantly sets Certified-Precision diffraction grating to desired wavelength; no color filters to fuss with.
- **FASTEST READING!** Instant-acting meter gives exact percent transmission, or optical density.
- **LOW PRICE, DOUBLE VALUE!** Colorimeter *plus* spectrophotometer, 375mμ-950mμ range in one long-life, trouble-free instrument. (Extended range, 340mμ-950mμ at slight extra cost.)

Used in these and many other industries
to maintain quality and boost output:

METALS RUBBER PETROLEUM FOODS PLASTICS
PAINTS PLATING LEATHER DYES PAPER BEVERAGES
TEXTILES PHARMACEUTICALS SYNTHETIC FIBERS

MAIL COUPON FOR IMPORTANT DATA

BAUSCH & LOMB OPTICAL CO.
64239 St. Paul St., Rochester 2, N. Y.

☐ Send me B&L Spectronic 20 Catalog D-266.
☐ I would like an obligation-free demonstration of the B&L Spectronic 20 Colorimeter at my convenience.

Name ..... Title .....
Company .....
Address .....
City ..... Zone .... State .....

13 March 1959, Volume 129, Number 3350 SCIENCE

Organization of Science in the United Kingdom

There are significant differences as well as similarities between U.K. and U.S. national science patterns.

E. S. Hiscocks

In this article I shall not attempt to give a detailed picture of the organization of science in Britain but rather to sketch in some of the principal features of the British setup and to indicate the manner in which these differ from, or are similar to, the pattern in the United States.

In order to get our sights adjusted I should, perhaps, remind you that the population and area of the United States are about 3.3 times and 38 times, respectively, the population and area of the United Kingdom.

Unfortunately there are no authoritative up-to-date and comparable figures for expenditure on research and development in the two countries, but in 1957 expenditure in the United States was probably about $7 billion and in the United Kingdom, about £350 million. Each of these figures is very nearly 1.6 percent of the gross national product, and—although my figures are subject to correction—it is, I think, fairly clear that, on this basis, the scales of expenditure on research and development in the two countries are of the same order.

It is when we examine the sources of these vast sums that differences emerge. In the case of the United States, it is probable that about 50 percent of the total is government expenditure, whereas the corresponding figure for the United Kingdom is probably about 75 percent. Thus, government looms much larger in the United Kingdom science picture than it does here.

Now let us consider the United Kingdom picture in somewhat greater detail.

Industry. Although it can be deduced that expenditure on research and development by private industry is significantly less in the United Kingdom than in the United States, the pattern and objectives are much the same except in one important respect (the Research Associations), which I will refer to later.

Government. Here the organizational pictures differ from each other; Fig. 1 gives a highly simplified representation of the British organization.

Defense Research

The right-hand section of Fig. 1 represents defense research. Although defense research runs away with so much of the money, its organization and objectives are fairly obvious. Defense research is, of course, aimed primarily at satisfying the requirements of the defense departments; it is largely concentrated, as far as the Navy is concerned, in the hands of the Royal Naval Scientific Service (this is a civilian service), and as far as the Army and Air Force are concerned, in the Ministry of Supply, which is a civilian department set up during World War II to satisfy the requirements of the War Office and the Air Ministry.

A substantial amount of this defense work has important civil applications. Examples of this are the work of the National Institute of Oceanography, which is controlled by the Admiralty; the Royal Aircraft Establishment (the largest scientific establishment in the United Kingdom), which is controlled by the Ministry of Supply; and the Meteorological Office, which is controlled by the Air Ministry.

Civil Research before 1914

Although the association of government and science in the United Kingdom goes back for some hundreds of years, official interest in science before the present century was confined almost wholly to the direct requirements of the administration or the defense of the realm. Thus, in 1675, Charles II established the Royal Observatory at Greenwich, so that tables of the position of the moon and the fixed stars could be corrected "for the use of his seamen." The Geological Survey was founded in 1835, and the Meteorological Office, in 1854, but it was not until the closing years of the 19th century that the Government was made to realize that science had something to contribute to the general welfare of the nation.

This came about, at least in part, through the efforts of the British Association for the Advancement of Science, which asked itself why Germany was beginning to oust the United Kingdom as the foremost manufacturing nation in Europe and decided that one reason, at least, was that the German Government was supporting scientific work in such establishments as the Physikalische Technische Reichsanstalt. After some years of agitation and negotiation, a small grant of government money and Queen

The author is director of the United Kingdom Scientific Mission and scientific attaché of the British Embassy, Washington, D.C. This article is adapted from an address delivered 26 Dec. 1958 before a symposium, "Moving Frontiers of Science: Comparative Patterns of Scientific Organization," held during the Washington meeting of the AAAS. This article and the following one, by Robert Major, were presented during part 1 of the symposium. The papers presented during part 2 will appear in next week's issue.

Victoria's agreement to the use of Bushy House were obtained to enable the Royal Society to found the National Physical Laboratory. This laboratory came into being on 1 January 1900 (and was, by the way, followed by the third great standards laboratory—your National Bureau of Standards—about 1½ years later).

(The British Association, which is our equivalent of the American Association for the Advancement of Science, has, by the way, during its 127 years of life, played an important part in keeping the country informed on the aims and achievements of science. Man has released vast forces of nature which he is still struggling to control. An understanding of these and of the possibility of using them for the benefit of mankind is necessary for every thinking person who wishes to understand the contemporary scene.)

Although the formal terms of reference of the National Physical Laboratory covered only the testing of instruments and materials, a strangely prophetic speech was made by the Prince of Wales (later King George V) in 1902, at the opening of the laboratory's then new engineering building, when he said:

"I believe that in the National Physical Laboratory we have the first instance of the State taking part in scientific research. The object of the scheme is, I understand, to bring scientific knowledge to bear practically upon our everyday industrial and commercial life, to break down the barrier between theory and practice, to effect a union between science and commerce."

Although we are now familiar with such ideas, they were quite revolutionary 57 years ago. From 1909 on, however, the Government assumed a wider responsibility for promoting and encouraging scientific research, and since that time the form and extent of government assistance have been adapted to meet the rapidly changing conditions in industry and education. Even so, the Government worked mainly through grants to committees and learned societies until the importance of scientific research was emphasized by the lessons of World War I.

General Coordination of Government Research

Before the emergence of cabinet government in the 18th century, the chief source of executive power in Great Britain was the Privy Council. The Privy Council Office still exists and is controlled by a senior cabinet member, the Lord President of the Council. When research councils were established they operated under committees of the Privy Council, and we have a situation in which the Lord President, who is, therefore, responsible to Parliament for the work of the research councils, has come to be regarded as having a general oversight of scientific matters.

At the end of World War II, the Government established an Advisory Council on Scientific Policy to advise the Lord President on his various scientific responsibilities. The Minister of Defence is advised by a parallel committee—the Defence Research Policy Committee—and some members are common to the two committees.

Civil Research after 1914

In 1916, the Department of Scientific and Industrial Research was established as a separate government department. Financial control of the National Physical Laboratory was transferred to this department, although the "management" of the laboratory's scientific work still remains the responsibility of the Royal Society. The Department of Scientific and Industrial Research now has 14 research stations (for example, Geological Survey, Road Research, and Radio Research) and is associated with the setting up and operation of 46 industrial Research Associations. It also administers an Overseas Liaison Division, which services the scientific attaché program. Hence, my administrative base is the Department of Scientific and Industrial Research, although I do not by any means spend the greater part of my time on matters of concern to that department.

The Department of Scientific and Industrial Research is a full department of state and operates directly under an executive council known as the Research Council. The department's senior officers are scientists, and all its secretaries (the title by which the permanent heads of most British Government departments are known) have, with the exception of the first, been eminent scientists such as Sir Henry Tizard and Sir Edward Appleton. There is no strict parallel to this department in the American scientific scene, although the National Science Foundation fulfills here many of the functions of the Department of Scientific and Industrial Research in the United Kingdom; however, the National Science Foundation does not run its own laboratories.

One factor in the operation of the department is of particular interest. It works on a quinquennial basis in regard to financial and staff allocations, because it is recognized that a year is now an insufficient period of time for the successful planning and completion of scientific work and for the manufacture of expensive research tools—for example, the National Physical Laboratory ship tank.

The Medical Research Council and the Agricultural Research Council were created in 1920 and 1931, respectively. These councils also operate laboratories, maintain research units at universities, and make research grants. They differ, however, from the Department of Scientific and Industrial Research in that they obtain their funds by grant-in-aid and not on a direct parliamentary vote. This means that the councils have considerable freedom within the limits of total funds made available and that they are not subject to direct departmental control.

Many of the executive departments of state have scientific advisers, and some operate their own laboratories—for example, the Post Office and the Home Office (the counterpart of the U.S. Department of the Interior).

Atomic Energy

Prior to 1957, the Lord President was also responsible to Parliament for atomic energy policy in general. In April 1957, the Lord President's responsibility was transferred, by Order in Council, to the Prime Minister. The development of new sources of energy for peaceful purposes is of the highest economic importance in the United Kingdom because of our lack of indigenous fuels.

Research on both civil and military applications of atomic energy is carried out in the main by the Atomic Energy Authority itself. The Authority, which was established as a public corporation by act of Parliament in 1954, has quasi-governmental status and is subject to broad but not day-to-day government control.

Thus we now have the following situation:

1) The Lord President, a senior member of the Cabinet, is responsible for the formulation and execution of government scientific policy; for the operation

of the three research councils responsible for agricultural, medical, and scientific and industrial research, respectively; and for operation of the nature conservancy program.

2) The Prime Minister has himself assumed responsibility to Parliament for atomic energy policy in general.

3) Other ministers have responsibility for the scientific establishments within their own departments.

4) The advice of the research councils is at the disposal of the executive departments, and there is close liaison between them, but the research councils are *not* subject to departmental control.

In view of suggestions, both in the United Kingdom and in the United States, favoring the setting up of ministries of science, a recent comment by Lord Halsbury regarding the United Kingdom is of interest. He stated that, since the cost of government science is small in relation both to its importance and to the over-all budget, there are good arguments for making it a part-time responsibility of a senior member of the cabinet rather than the whole-time responsibility of a junior member.

Scientific Civil Service

So much for the organization in Government. Now, what about the people who do its scientific work? In the main, this falls to the Scientific Civil Service. Although scientists have been employed in the civil service for many years (I myself have been a scientist in the civil service for 30 years), the Scientific Civil Service, as such, came into being only in 1946. It was created so that reasonable uniformity in standards of qualification, performance of work, promotion prospects, and so on could be achieved. Re-

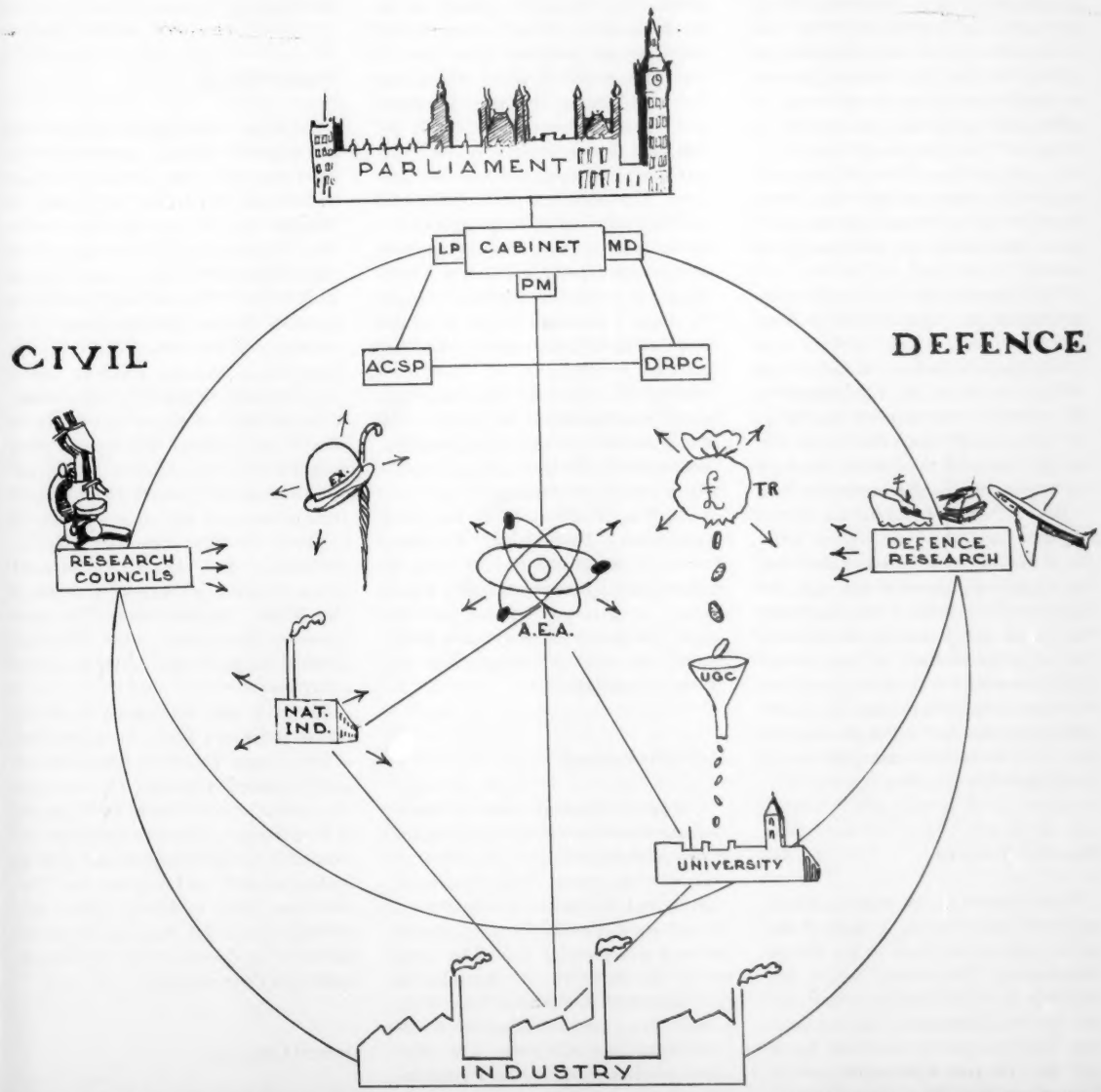


Fig. 1. British governmental organization for scientific research. ACSP, Advisory Council on Scientific Policy; A.E.A., Atomic Energy Authority; DRPC, Defence Research Policy Committee; EX., Executive departments; LP, Lord President of the Council; MD, Minister of Defence; NAT. IND., Nationalized Industries; PM, Prime Minister; TR, Treasury; UGC, University Grants Committee.

cruitment to established posts is through the Civil Service Commission's Scientific Branch, which acts as a recruitment and qualifying agency but does not, as does its counterpart in the United States (I believe), deal with rates of pay and conditions of service. These are the province of the Treasury in the United Kingdom.

There are three main classes in the Scientific Civil Service, and many specialist classes. The three main classes are as follows: Scientific Officer—the initiators; Experimental Officer—the doers; and Assistant (Scientific)—the helpers.

The over-all numerical ratios of members of these classes in the service is approximately 1:2:1. Promotion is by merit, and in the Scientific Officer class it can either be up the organizational ladder, so that the scientist assumes greater responsibility for the work of others as he progresses, or it can be up the "merit" ladder so that he can achieve high rank purely on his excellence as an individual scientist. In my view, this is one of the most significant developments in the employment of scientists in the postwar era.

This three-tier structure parallels the structure of the General United Kingdom Civil Service, with its three main classes: administrative, executive, and clerical. In Britain the administrator is the person who makes policy; the executive is the person who carries it out. You will see from this that we use the term *executive* somewhat differently from you.

The difference between the British structure and American two-tier structure is probably more apparent than real, but up to the present, in any case, the Scientific Civil Service has steadfastly maintained that possession of university degrees is not of itself an open-sesame to the Scientific Officer class. In my last laboratory, some 30 percent of the experimental class had university degrees, and many more had other professional qualifications.

Industrial Research

Public authorities. A group warranting brief consideration is that of the public corporations, such as the British Broadcasting Corporation, which are subject to broad but not day-to-day control by the Government. The nationalized industries, such as the Coal Board and the Transport Commission, are in the same position. All of these organizations carry out research themselves and maintain close liaison with the research councils and departmental research organizations. The special case of the Atomic Energy Authority was referred to earlier.

Research Associations. A feature of British research is the part played by Government in cooperative industrial research. There are 46 of these autonomous organizations of industrial firms which carry out research of concern to the participating industries. Their establishment is voluntary in the sense that the initial proposal must come from industry itself. They are governed by their own councils, the members of which are drawn mainly from the industry concerned. The councils are advised by research committees in the preparation of their research programs. They have a combined income of about £7 million, about one-quarter of which is contributed by the Government through the Industrial Grants Committee of the Department of Scientific and Industrial Research. Curiously enough, the large corporations which spend large sums on scientific research are also, in general, strong supporters of the Research Associations, whereas it was originally thought that these associations would be of use mainly to small firms unable to carry out their own research.

Sponsored research. Sponsored research organizations of the pattern and size of certain American organizations do not exist in the United Kingdom, although there are three small units, one of which is an offshoot of an American organization. The United Kingdom, however, just like the United States, is rich in independent organizations which finance or carry out research—for example, the British Empire Cancer Foundation, the Lister Institute, and the Nuffield Foundation.

University Research

The most important source of fundamental research in the United Kingdom is the universities. About 70 percent of their income comes from government sources, and this money is administered through the University Grants Committee on a quinquennial basis. The members of this committee are appointed by the Chancellor of the Exchequer from persons with experience of university administration and education. The committee receives its money as a grant-in-aid and is responsible for allocating it to the universities. This system ensures academic freedom, since there is no direct departmental control of the distribution of the funds.

Research is also supported in the universities by the research councils (scientific and industrial; agricultural; and medical) and by industrial organizations which provide research fellowships and occasionally endow chairs.

All research funds are administered so as to interfere as little as possible with academic freedom. There is relatively little contract research in British universities, and my own experience has been that any proposal which might even appear to curb this freedom meets with immediate and effective opposition from the faculties.

Learned Societies

No picture of the British research setup is complete without mention of the learned societies, the foremost of which is the Royal Society. In 1663, Hooke (of "Hooke's Law" fame) wrote that the society's business was "To improve the knowledge of all natural things, and all Useful Arts, Manufactures, Mechanick Practices, Engines and Inventions by Experiment (not meddling with Divinity, Metaphysics, Moralls, Politicks, Grammar, Rhetoric or Logick)." The society is independent of state control, but its advice on scientific matters is often sought by the Government. It also administers various research funds derived from government and other sources.

There are many other scientific organizations which should be mentioned in any reasonably complete account of the British scientific scene. They are, however, so numerous that to name them would make this article read like a directory.

There is one committee, however, which, as far as I know, has no parallel in this country. This is the Parliamentary and Scientific Committee. This committee consists of members of both Houses of Parliament, of all parties, who are interested in scientific matters and also of leading scientists and technologists. The committee meets to discuss science and scientific matters and thus helps to maintain in the legislature a body of informed opinion on these matters.

General Comments

I have tried to give a picture of the main elements of scientific organization in Great Britain. It is a picture which

is changing in detail from year to year to meet the changing requirements and the ever-increasing importance of science in all aspects of national life.

A great—perhaps too great—proportion of our scientific effort is devoted to fundamental research. This is due to many causes, one of which is the educational system, which tends in science to produce rather narrow specialists. In our secondary schools we do not give one-year courses in such subjects as biology but prefer, from age 11 on, to rely on a three-year course in general science followed by continuous courses for the next four years in major branches of science. Students intending to go to a university normally take the Advanced Certificate of Education in three subjects at age 18.

In this connection it is interesting to note that in 1957 more students sat for this examination in physics, chemistry, and mathematics (in that order) than in any other subjects and that nearly 20 percent of all students took physics.

This concentration on few subjects continues in the universities, which are staffed in the main by people chosen for their skill in basic research rather than for their skill in teaching, and the universities do relatively little sponsored work.

Efforts are now being made in several British universities to broaden the educational basis, and my personal view is that there is much to be said for the system about halfway between your system and ours.

Finally, our social structure is such that attainment in pure science appears to attract greater social status than attainment in technology—we revere our eggheads! On the other hand, we have a great need for application of science, and the Government is now taking great pains to increase the output of technologists—not in the main, be it noted, in the universities but in technical colleges and special Colleges of Advanced Technology (these grant diplomas but not the traditional university degrees).

On the government side we have a senior cabinet minister broadly responsible for much of the basic civil research. This minister is advised by a scientific policy committee which has some common membership with the corresponding committee which advises the Minister of Defence. We appear, therefore, to have a somewhat more closely coordinated system than exists in the United States. On the civil side research is mainly under the direction of scientists who are not subject to control by executive departments. We also allocate public money for basic research on a five-year basis, so as to give greater stability to our efforts.

This situation looks satisfactory but is by no means perfect and is not without its critics, who complain that no means exist either for formulating or for securing a coordinated national policy of research. Our educational system also comes in for criticism, especially from the point of view of lack of breadth in the education of scientists.

Again, although there is considerable direct cooperation in research between Government and industry, especially in the Research Associations, we do not appear, as a nation, to match up to the United States in practical application of the results. This is not wholly the fault of the scientists but is due also to economic and other factors.

Being a smaller and more closely knit country, we pay rather less respect than you do to the possession of formal qualifications. We tend to pay for ability and experience even though the latter may not have led to the gaining of higher degrees. We may, however, be changing somewhat in this respect.

Our government administrative processes seem on the whole to be more flexible than yours, and this difference stems no doubt, in the main, from our very different parliamentary systems. In yours, the executive and the legislature may not always see eye to eye. In ours, the Cabinet represents the majority party in Parliament. It also possibly stems from the traditional reluctance of British administrators to specify and define more closely than is absolutely necessary. (You have a written constitution—we haven't). However, when all is said and done, our outlook and aims are much the same as yours. Cooperation between American and British science is close, and I regard it as one of my principal objectives in my capacity as scientific attaché here to improve and extend this cooperation in every way possible.

There is an old saying that "comparisons are odious," and in making comparisons I have not been trying to show that the methods of one country are in general superior to those of the other. It is fairly evident that we can each learn from the other and that in at least one important instance—that of education—a midway course would be of advantage to each of us. Some of the differences are more apparent than real. I have on many occasions been present at discussions between British and American scientists about their difficulties and hopes when it would have been very difficult for a man from Mars to tell which were British and which American!

Probably in no other major field of human endeavor is it so necessary to consider the individual and to try to fit the organization to the men rather than the men to the organization.

Organization and administration in science are a means to an end, and in conclusion, therefore, I would like to quote a British scientist and our leading humorous journal.

The scientist, Sir Ben Lockspeiser, a former secretary of the Department of Scientific and Industrial Research, said at the end of a lecture, "Let me therefore conclude by underlining the importance of good administration, but by reminding you also that administration in science will not, of itself, produce a single new idea and without new ideas science would cease to exist."

The journal is *Punch*, which 22 years ago said, "The greatest of all research problems is the people who do the research."

Organization of Scientific Activities in Norway

Government, industry, and research have joined forces to develop the country's research capacity.

Robert Major

Norway, which has only 1/25 the area and 1/50 the population of the United States, is by far the smallest of the four countries to be reviewed in this series of articles. I do not know why my country has had the honor of being selected as one of the four, but sometimes it is easier to study principles on a small scale, and this fact may perhaps justify the inclusion of Norway. The population of Norway is about 3.5 million. Almost three-fourths of the country consists of mountains, glaciers, and so on; approximately one-fourth is covered by forests; and only 4 percent is tilled soil. Thanks to the Gulf Stream, coming over from the Gulf of Mexico up along the coast line, the climate is much warmer than you would expect.

Norway does not have the same old well-established scientific traditions that are found in many other European countries. This is probably partly due to the size of the country, but also to the fact that Norway, when it became an independent country in 1905, had not had complete independence for several centuries.

Our first university was established only some 150 years ago; our Agricultural College, some 60 years ago; the Institute of Technology, some 50 years ago; and our second university only 10 years ago. The period prior to World War I can be characterized by the outstanding work of some few individuals within certain fields of the humanities, medicine, and science. The environment for research was, however, too narrow, and our economic resources were too limited for lasting, learned schools to grow up, except in a few fields such as, for instance, geophysics. Research in the industrial field showed the same tendency. Comparatively few companies carried out their own research. Nevertheless, some examples of outstanding work were produced, and some of our leading firms of today were built up at that time entirely from the results of research work.

Between the two world wars scientific life in Norway had a constant but not rapid growth, both in the fundamental and in the applied fields.

During World War II, however, when the scientific resources of the three other countries considered in these articles were mobilized to the utmost and when their institutions for applied research had a time of fantastic expansion, Norway had a very different experience. Our universities were partly closed and our scientific activities came nearly to a standstill. The only bright spot was a small group of Norwegian refugee scientists who took part in military research in Great Britain and later became the nucleus of the Norwegian Defense Research Establishment which was built after the war.

When the war was over, however, it was clear to our Government, to industry, and to all within the research field that very high priority had to be given to the expansion of research. Thanks to excellent cooperation among these parties, this expansion has taken place.

Trades and Industries

As the development since the war has been strongest in applied research, I shall first, for background purposes, say a few words about the trades and industries of the country.

From Fig. 1 you will see that by far our biggest economic factor is industry, and that industrialization proceeds at a good rate of progress. One of our greatest assets here is the abundance of cheap water power. Norway produces today per capita more energy in the form of electricity than any other country, and we can still triple or quadruple this production at a very low cost. This is a great advantage from the standpoint of further development, especially within the electrometallurgical and electrochemical industries.

Shipping constitutes a major and growing factor in our national economy. Norway currently provides 8 percent of the world's tonnage. This has also stimulated growth of the Norwegian shipbuilding industry, which has more than tripled since the war.

Investment in the building of houses, factories, and power plants is at a high level.

Organization for Research

Let us now look at the pattern of research institutions as they have developed thus far. Figure 2 gives, in a simplified form, a survey of the various types of research organizations and institutes. To the left we have the universities, which come under the Ministry of Education. Next we have the various governmental research institutes, coming administratively directly under their respective ministries and working in such special fields as mineral resources, agriculture, fishery, health, communication, and defense. To the right we have the institutes which belong to industry. They comprise both the individual companies' own laboratories and the institutes of research associations formed by special branches of industry. In the middle you will see the research councils. There are three of them. All three have been established since the war, and they represent an entirely new feature in our scientific life. There are also other institutions which have been omitted here in order not to make the picture too complex.

As you can see, this general pattern is not so very different from that found in most other modern countries. There are, however, certain distinctive characteristics which I will try to point out.

Mr. Major is director of the Royal Norwegian Council for Scientific and Industrial Research. This article is adapted from an address delivered 26 Dec. 1958 at a symposium, "Moving Frontiers of Science: Comparative Patterns of Scientific Organization," held during the Washington meeting of the AAAS. This article and the preceding one, by E. S. Hiscocks, were presented during part 1 of the symposium. The articles presented during part 2 will appear in next week's issue.

Universities

The universities in Norway are all governmental universities. This means that they get practically all their money from the national budget, the number of positions and the salaries are established by the Parliament, and all the professors are appointed by the Government on the advice of the universities. By *universities* I mean here the two universities proper, in Oslo and Bergen, and also such institutes of higher learning as the Norwegian Institute of Technology in Trondheim, the Agricultural College at Aas, just south of Oslo, and the School of Business Administration in Bergen, which all give degrees that are at the university level.

As in most countries, in addition to their educational activities the universities carry the main burden of fundamental research work. The national appropriations alone have always been too small to maintain a vigorous scientific life, but research work has also been partly financed by private endowments and through contracts with industry and trades. Since the war a great proportion of the basic and other research at the universities has been financed through grants from the research councils.

The universities have also attracted other institutes as neighbors, thus making four major centers of research in the country. There is a center of technology around the Institute of Technology in Trondheim, a center of fishery research (among others) in Bergen, a center of agricultural research at Aas, and a center covering other fields, such as humanistic, economic, social, medical, and industrial research, in Oslo.

A special feature in Trondheim deserves to be mentioned; there an Engineering Research Foundation has been established at the Institute of Technology, doing sponsored research for industry in cooperation with the institute. This foundation has a much more flexible organization than the Institute of Technology and has therefore also been able to support the institute in many administrative matters.

As in so many other countries, there was a great increase in the number of students entering our universities just after the war. By 1954, however, the number had fallen to the prewar level, and it only started to rise again substantially last fall. To get the complete picture, however, we must take into consideration the fact that since the war some 25 percent of our students have taken their degrees abroad because of our own limited study facilities in such fields as engineering, medicine, and dentistry.

	1938	1948	1957 ESTIMATE
	%	%	%
Industry and mining	24.6	25.7	29.2
Agriculture and forestry	11.1	8.0	6.8
Shipping	9.8	7.8	9.9
Building and construction	5.5	6.7	7.0
Others	49.0	51.8	47.1
	100.0	100.0	100.0

Fig. 1. Gross national product by sector (fixed prices).

As the demand and supply of scientists and engineers have been so much discussed lately, I will say a few words about our experience in these fields. It has, I think, some unique features.

Our only institution for the education of engineers is the Institute of Technology in Trondheim. Because it was in bad shape after the war, we sent a lot of engineering students abroad for their training. This stream of students going to other countries has continued, because of limited capacity at home. In fact, during the last few years nearly 50 percent of our engineers have been educated abroad. We have thus arrived at a total figure per million inhabitants of 130 new engineers per year, with a degree corresponding to an average American master's degree. This is, I think, the highest figure in Europe. In viewing this, however, our present low production of pure scientists and technicians should be noted. The engineers have all been absorbed in industry and research, and a study of the supply and demand made by the Research Council has concluded that our demand will continue at this level in the coming years. Accordingly, the Institute of Technology in Trondheim is being nearly doubled in size, and by 1963 we expect to turn out some 80 percent of our engineers at home, relying on institutions abroad only for the education of engineers in a few specialties. However, much work still remains

1946:	1100	340	0	58	?
1958:	1800	1180	1089	250	?

Fig. 2. Over-all research organization. Figures give total number of personnel.

to be done to build up the graduate school in Trondheim.

For scientists the picture has been very different. Pure science is an unrestricted study, and the universities accept all the qualified students who want to study science. Since the war the number of candidates has been fairly constant but comprises only some 65 percent of the number required, on the basis of a conservative estimate, to meet Norway's needs. Among other problems this created a serious, increasing shortage of science teachers in the secondary schools. The situation thus became rather gloomy.

Last summer, however, the curriculum of the science department of the university was modernized. An attempt was made to make the study more effective and thereby shorten the time of study from an average of 7 or 8 to 5½ years. This change was made known to all potential science students, and at the same time they were informed of the career possibilities for a student of science. Although a modest increase in the number of science students was expected, we were surprised to find that the number of science freshmen last fall rose by more than 100 percent; this means a tripling over the last two years. This very encouraging development has, however, its darker aspect. Now the great difficulty is for a somewhat unprepared university to find ways to educate so many students in rather crowded and inadequately equipped departments.

On the whole, I think we must admit that although it now looks as if we shall get out of our scientific and technical manpower problems reasonably well, this will perhaps be due more to the initiative of our youth and to help from universities abroad than to our own ability to build up our higher education in time. Recent developments, however, seem to indicate that planning and development of our institutions will be more efficient in the future.

The facts which I have given seem to show that most of our universities have not been farsighted enough to adapt their activities to the needs of the future. There may be many reasons for this. I think our system is somewhat too rigid; there is lack of flexibility and too great a distribution of responsibilities. Much good work is being done, but it is my personal view that the building up of a stronger administration in the universities—an administration capable of taking and willing to take responsibility—is a necessary step to insure that the universities will be able to play their vital role in the future life of the nation.

A thorough study of the demand for and supply of university-trained personnel of all categories has lately been made by our research councils. The aim of this has been to establish a factual basis for the development of our academic institutions to fill the future needs of the country.

Before leaving the field of training I will mention one noteworthy organization, the Government Loan Fund for Students. Because most families now find it difficult to finance the studies of their children, a national loan fund for students has been organized, with considerable capital and a further government guarantee. At present more than half of all Norwegian university students at home and abroad have loans averaging 3000 kroner a year. They pay no interest during the time of their study and later can deduct from their taxable income the money they pay back. Through growing fellowship programs gifted students without financial resources are also stimulated to take up a study.

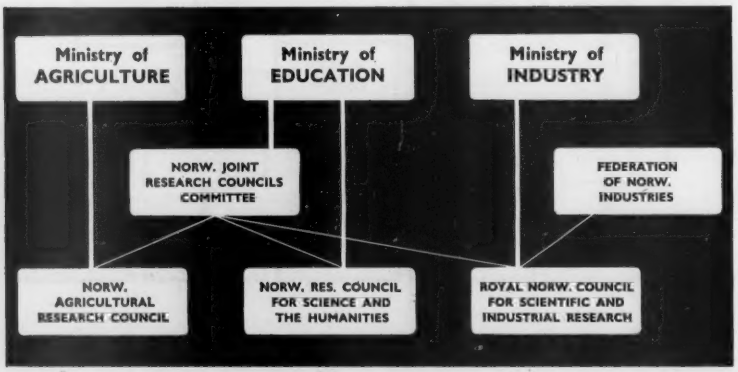


Fig. 3. Research councils in Norway.

Government Research Institutes

The government research institutes under the different ministries do not differ in principle from those in other countries. Therefore, although they play an important role, I shall be very brief in discussing them. The advantage of these institutes is, of course, that they have a reasonably secure source of income. On the other hand, they have a very rigid salary system, so it is difficult to maintain a sufficient degree of incentive throughout the system. These are all difficulties which you seem to be well aware of in the United States, where, to a great extent, you get around them by doing a great deal of this sort of work through government contracts to universities, to sponsored research institutes, and to industry.

I have already mentioned the fields in which these institutes work. They have all expanded considerably since the war; this is particularly true of the Defense Research Establishment, which was established at the end of the war and which has since grown to become our biggest research institute. It has more flexibility than is usual for government institutes.

Research in Industry

In industry the interest in research activities has developed at quite a good rate since the war. Research departments and laboratories have grown up in many of the bigger companies and are now being introduced in new factories, but we still have a long way to go to reach an activity comparable to industrial research in the United States. One reason is that we have relatively few companies which are big enough to finance research on a really grand scale.

A statistical study of research personnel and research expenditure in industrial companies is now in preparation, but figures will not be available until the spring of 1959.

Some branches of industry have formed research associations for cooperative research studies. There are now ten of them, the biggest being in the fields of paper and pulp, wood technology, canning, herring oil and meal, and textiles. In many branches the size of the companies varies so much, and the technical interests are so heterogeneous, that research associations are not the right answer. These factories rely on sponsored research institutes for work which they

cannot undertake themselves (I refer to this below). One characteristic feature is that a very good contact has been established between industry and the various research institutes, and industry is using their services more and more.

It is the general rule in our country that results of industrial research are exploited in already existing companies. Lately, however, a few development companies have been established which specialize in the exploitation of research results. This work looks quite promising so far.

Quite recently industry has formed a new organization called the Norwegian Industries Research Association. This is an organization with the single aim of supporting financially research work of common interest to the member firms. It is an organization set up on a voluntary basis, and all the firms joining it give 0.3 percent of their gross sales receipts to the association every year. All the money of the organization is being used for projects suggested by the Research Council for Scientific and Industrial Research, mentioned below. The association started to operate last fall; most of the bigger companies have joined it, but to get the great bulk of the smaller companies as members remains to be accomplished.

In this connection, I should mention that we have in Norway a law allowing firms to deduct from their taxable income gifts to research institutions. This, however, applies only for gifts not exceeding 10 percent of their income. The research must also have some bearing on the activities of the firm and must be carried out by an institution having some connection with the Government.

Research Councils

A new feature in Norwegian research organization since the war is the establishment of research councils. As you will see from Fig. 3, there are three of them: the Royal Norwegian Council for Scientific and Industrial Research; the Norwegian Research Council for Science and the Humanities; and the Agricultural Research Council of Norway. They all have the task of promoting research within their respective fields. They have come to play a very active part in the scientific life of Norway since the war, and they are also known for the rather extraordinary way in which they get a good deal of their money—from the profits of football pools.

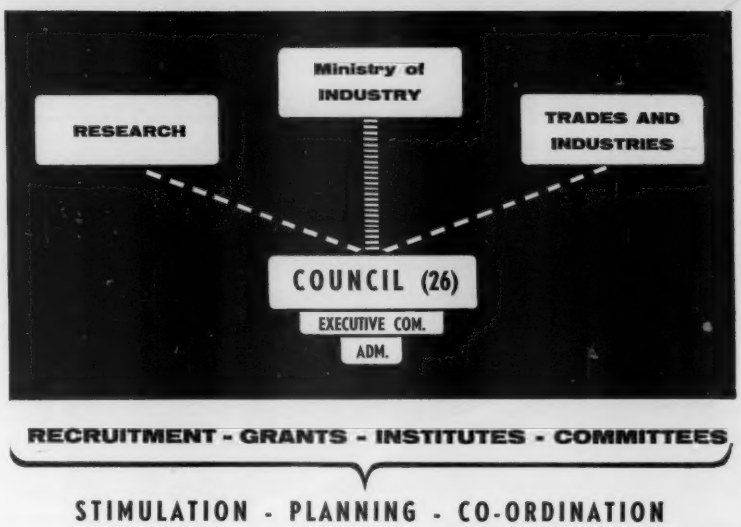


Fig. 4. Organization of the Royal Norwegian Council for Scientific and Industrial Research.

Just after the war the football pools were organized as a semigovernmental company with the aim of supporting sports and research. Of the profits, the first million kroner go to sports. Of the second million, research gets 200,000 kroner; of the third, 400,000 kroner; of the next, 600,000 kroner; and of each additional million, 800,000 kroner. Last year the amount for research had thus increased to some 25 million kroner. The amount is distributed among the three councils through the Joint Committee of the Norwegian Research Councils. The amount is quite appreciable for a small country, but the really important factor is that the money can be used at the discretion of the research councils.

I cannot here go into details about all the councils. I will say only that the Research Council for Science and the Humanities, through grants in all fields of the humanities, medicine, social research, and fundamental science, has contributed greatly to research activities in these fields, while the Agricultural Research Council has, through its activities, stepped up research work in the whole agricultural field.

As an example of the three I shall give a few more details about the Royal Norwegian Council for Scientific and Industrial Research. I choose this because it was the first and is the most comprehensive of the research councils and also because it is with this council that I have had my own experiences.

From Fig. 4 you will see the main characteristics of its organization. It is a semigovernmental institution representing cooperation of government, industry, and research, with the aim of promoting scientific and industrial research and making sure that the research results are made use of in Norwegian trades and industries. The council has 26 members, with approximately equal representation from the three parties mentioned.

In summarizing the work of the Research Council, one should first mention the work done in the recruitment of scientific personnel. Surveys of the supply and estimates of the demand for scientists and engineers have been made, and recommendations for the expansion of our capacity for education have been made to the Government. To support the flow of promising candidates into science, approximately 250 fellowships have been given for postgraduate studies in foreign countries. Fellowships have also been given for postgraduate work in our own country, both for Norwegian citizens and for foreigners wanting to take part in our activities.

Secondly, carefully selected research projects, mostly at the universities, are being supported through grants. The major part of these grants has been given in new fields such as nuclear physics, radiochemistry, industrial microbiology, and automation. They may be small grants for a personal assistant, for instance, or large ones for bigger, long-term projects, new buildings, and so on.

The council has, further, had a series

of committees fostering research in new fields where there was a need for organized long-term research. New institutes have been planned and established, 11 of them so far. Among them I can mention the Institute of Atomic Energy, which, in cooperation with the Netherlands, built the first nuclear reactor to be in operation outside the borders of the five big atomic powers. Very shortly the institute will put into operation the new heavy-water boiling reactor at Halden, which is the first nuclear reactor system to be developed outside the borders of the great atomic powers. Through cooperation with 12 other OEEC countries, the experiences achieved with this reactor system will be available to them all.

The council has also established institutes for building research, for geotechnical research, for ship and shipbuilding research, for electrotechnical research, and so on. They are all institutes of particular interest to important branches of our industries. I might further specifically mention the Central Institute for Industrial Research, which is a sponsored research institute, built on the same principles as the Battelle Memorial Institute in Columbus, Ohio. The Central Institute is now one of our largest, and the number of contracts grows from year to year and also includes contracts from the United States.

As you know, you have in this country a great number of sponsored research institutes, such as the Battelle Memorial Institute, and the Armour Research Institute, but relatively few research associations for cooperative research. In most European countries—for instance, in Great Britain—there are a great number of cooperative research institutes but practically no sponsored research institutes. In Norway we now have three sponsored research institutes; the volume of research in these institutes is about the same as the volume in our cooperative research institutes, and it tends to grow faster.

In this respect we are thus somewhere between the United States and most European countries. We believe that in our country cooperative research is the effective solution for some activities, but we also feel that in other cases sponsored research is the best solution. To the cooperative research institute one sends bigger, open research projects of mutual interest; to the sponsored research institute a company sends research projects that it wants to develop for its own use in competition with others. The sponsored research institute functions, therefore, as an extension of the individual company's own research laboratories.

Through all its activities the Research Council endeavors to achieve a sound coordination of the over-all research activities of the country. As a concrete example of this I might mention the establishment of the Industrial Research Center at Blindern, near Oslo.

Just after the war, when the Research Council was planning some of its institutes, some other industrial research institutes were also being established. Since we are a small country, the Research Council felt that if these institutes were spread around at different places, none of them would be big enough to create a sufficiently creative scientific environment. Therefore, the council secured an area close to the science department of the University of Oslo, built a central building for the sponsored research institute mentioned above, where also smaller institutes could hire premises, and offered ground around the building to other institutes wanting to participate in the center. In doing this the council in no way tried to direct the work of the institutes but simply offered its services to bring them together and thereby facilitate collaboration.

The offer was so very favorably received that the Industrial Research Center is constantly growing and has at present 15 institutes. They are centered around the Central Institute for Industrial Research, which has been equipped with many sorts of expensive equipment, such as an electron microscope and spectrographs, which are used by all the institutes in the center. In this way excellent voluntary coordination both among the institutes and between the institutes and the science department has been achieved. At present about 40 million kroner have been invested in the center, and approximately 500 people work there.

The work of the council is financed through the national budget, the football pools, and industry. The council is a free institution with its own salary system, serving both government and industry. We have come to know the importance in all research work of choosing the right man for the job and of giving him a reasonably free hand. We emphasize strongly the importance of maintaining incentive for all personnel throughout the activities. The freedom we have been given, the flexibility of the system, and the great and united support from government, industry, and research have made it possible to build up a system which seems so far to have functioned reasonably well.

Government Research Contracts

But to come back to the over-all picture, there is one feature which you may miss in Norway—the government research contracts which play such an important role in the United States. In our country they are not used to any great extent. One reason is that problems of direct concern to government are solved in our governmental research institutes —such as, for instance, the Defense Research Establishment. Another reason may be that although it is difficult to carry out research, it is perhaps even more difficult to formulate research projects and evaluate research progress —and I think we have not yet a sufficient number of people capable of administrating research contracts.

There are, however, signs that this is changing, and with our growth in number of sponsored research institutes and in research facilities in industry I think it would be of advantage in the future to solve more national problems through research contracts with appropriate research institutions. It is not unlikely that the research councils may have a growing responsibility in this respect.

Problem of Size

We have also in our national research policy one problem which, I think, you are not very familiar with. That is what I may call the problem of being small. In these times, when each administrative unit, like each country, has so many research problems to tackle and when more and more of them are problems needing the concentrated attack of big scientific staffs, involving high expenditure, a small country meets with certain difficulties.

There are two ways of solving this problem. The one is to make use of the results from other countries when they are available and to concentrate our own efforts in areas where we have special qualifications or special needs. The other is to take up bigger projects in cooperation with one or more other countries, as we have done in atomic energy

with the Netherlands, Sweden, and other OEEC countries, in defense research and in fundamental nuclear physics through our participation in the CERN organization in Geneva. A closer cooperation between the Scandinavian countries in higher education and in many fields of research is also being developed.

What for you in the United States would usually be just routine cooperation will often for us be international cooperation, involving to some extent language and other difficulties. I do believe, however, that through concentration at home on the one hand and a realistic cooperation with foreign countries on the other, many of the difficulties of being small can be overcome.

From what I have said it will be evident that research activities have grown considerably in Norway since the war. Figure 5 shows the increase in the total number of individuals in university and other research work. The solid line indicates personnel in all kinds of research; the broken line shows personnel in scientific and industrial research only. Since we do not yet have exact figures for the individual companies' own research personnel, those figures are not included. You will see that from 1946 to 1958 the number of individuals in all kinds of research has grown by a factor of slightly less than 3. The biggest growth, however, has been in scientific and industrial research, where the number has grown by a factor of 4.

Figure 6 shows the expenditure in universities and research institutions, again with figures for the industrial companies' own research personnel excluded. You will see that in kroner the expenditure has grown by a factor of more than 6, but with fixed prices this factor is only approximately 4. For scientific and industrial research only, the rate of growth is somewhat larger.

You may now have got the impression that research is at a very high level in Norway. What the figures show is, however, more the rate of growth than the actual level. If we estimate the research expenditure of industrial companies and add this figure, we will find that what Norway spent in research and development in 1957 is not more than some 0.6 percent of its gross national product. This is less than half the corresponding figure for the United States and probably only one-third the corresponding figures for Great Britain and Canada. We may of course say that Norway is a small country and has not such great defense and other responsibilities and can therefore have a lower figure. Other factors, however, point in the opposite direction, so I believe that if we are to maintain our culture, our social standard, and our security, and have trades and industries which cannot only compete with those of Western countries but also withstand the growing commercial competition we have begun to experience from the Soviet

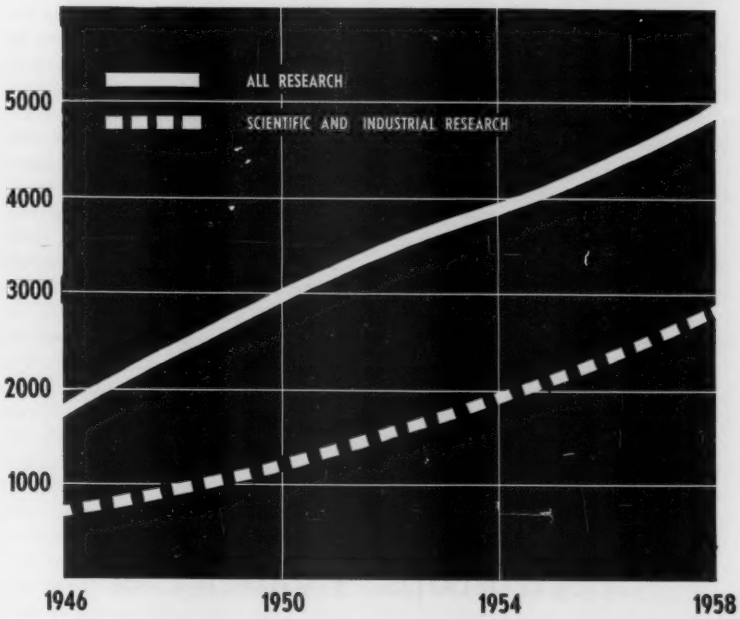


Fig. 5. Total number of personnel in research work, 1946–58. Universities, but not industrial laboratories, are included.

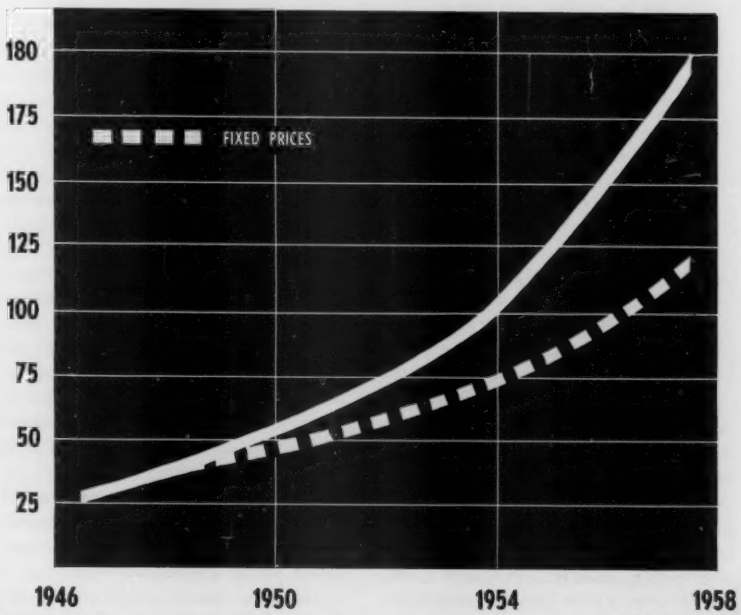


Fig. 6. Expenditure on research and development (in millions of kroner). Universities, but not industrial laboratories, are included.

Union, we must continue to expand our research.

There is also one new problem we have to face. It is probably right to assume that the attempt to create a free trade system in Europe, in spite of the present difficulties, will ultimately lead to a positive result. Although this as a whole must be favorably received, it will nevertheless create problems for certain branches of our industry. We must expect that some of these industries, now protected by customs duties, will be unable to compete in a free market. They will thus have to be replaced by industries in fields where we have special natural conditions—such as, for instance, the electrometallurgical and electrochemical fields. Since these particular industries, however, require heavy capital investments, we must also look for other possibilities. Here I think "brain" industries would be a good answer. To make such changes in our industries successfully, and in time, will require, to my way of thinking, some early and wise decisions in the fields of education and research.

Summary

By way of a summary, may I say that I believe we now have in Norway an over-all pattern for the administration of research which fits our present situation reasonably well. There are weaknesses, as I have pointed out, but there are also signs that we have a fair chance of putting them right. The system is sufficiently flexible to allow for initiative, and we know we shall have to make changes to fit our future needs. We are in the happy situation of having our youth show an increasing interest in research work, so if we can sucessfully master our training problems we should have the good recruitment we consider essential for progress in research. The problem of "being small" can probably be solved, or at least remedied, through a combination of concentration and international collaboration.

In think it has now become clear to the greater part of our population, and specifically to a great number of influential persons, that if we in Norway are to maintain and develop our spiritual and material culture, we shall have to continue the progress in research. We thus hope that in the future, through a united effort of our Government, our trades and industries, and our research, we shall be able to contribute our share to the common fund of knowledge and shall be able also to use this knowledge to expand the social and economic life of our nation and contribute to the security of all free nations.

Spectroscopic Evidence of Metabolic Control

Rapid measurements of intracellular events afford new evidence on mechanisms for metabolic control.

Britton Chance and Benno Hess

The interaction of glucose and oxygen metabolism has been the subject of study ever since Pasteur's discovery 100 years ago of the metabolic response of glucose utilization which now bears his name (see *1, 2*). Recent interest has been stimulated by Warburg's hypothesis that irreversible damage to the respiratory mechanism and a consequent increase of glycolysis are associated with cancerous growth (*3*). With greater knowledge of the enzymatic pathways for glucose and oxygen metabolism and of the significance of intracellular levels of substrates, coenzymes, phosphate, and adenosine phosphates, general principles and specific mechanisms for the Pasteur reaction (*4–11*) have been proposed. Increasing awareness of the structural relationships of enzyme systems within the cell (*11, 12*) adds, however, to the problem of ordinary chemical analysis a dimension with which it is not currently able to cope, namely, the control of metabolism by redistribution of rate-limiting substances among the intracellular structures. Such changes in concentration might well remain undetected in chemical analyses of the average concentration of such components (*2, 11*). It is an appropriate time, therefore, to describe results of the measurements of changes of concentrations of possible control substances at the site of their action within the cell.

The development of methods for the direct spectrophotometry of intracellular respiratory pigments and their applications to the measurements of the kinetics of oxidation of cytochromes, flavoprotein, and pyridine nucleotide, together with the adaptation of rapid flow techniques to rapid reaction kinetics of intact cells, were described several years ago (*13*). The advantages of ascites tumor cell suspensions for experimental study with these new methods have been pointed out from the standpoint of physiology and biochemistry (*3, 14*) and also from the standpoint of the requirements of the spectrophotometric technique (*13*). It has further been found that ascites tumor cells are remarkable material for the study of interactions between glucose and oxygen utilization, overbalanced in favor of glycolysis. The cells furthermore show not only a Pasteur and a Crabtree effect (*15*), but also a short-lived and intense metabolic response to glucose addition which sheds considerable light on possible mechanisms of metabolic regulation (*16*).

Even though it was suggested some time ago (*17*) that it is not the enzymes but their interactions that are responsible for tumor cell metabolism, explanations for the relatively low respiratory activity of some types of tumor cells have been advanced on the basis of low cytochrome *c* and low cytochrome oxidase activities (for a summary, see *18*).

Dr. Chance is director of the Johnson Research Foundation, School of Medicine, University of Pennsylvania, Philadelphia. Docent Hess is a member of the Medical Clinic, University of Heidelberg, Heidelberg, Germany.

Recently Warburg has proposed damage to the respiratory system (*3*). However, spectrophotometric studies of cytochromes of the ascites tumor cell show no deficiency of cytochrome *c* relative to cytochrome oxidase (*19*) and no damage to the respiratory carriers (*16*). This conclusion is so greatly at variance with the chemical determination of cytochrome *c* and cytochrome oxidase activities by extraction procedures in various types of tumor material that further study of the nature of the respiratory chain in the ascites tumor cell is reported here. The pathway of electron transfer, both in the intact cell and in the mitochondria isolated therefrom, has been investigated, and quantitative studies of the cytochromes of the cell and of the mitochondria have been made. These results clearly indicate the high capabilities of the respiratory chain of the ascites tumor cell for rapid electron transfer and efficient phosphorylation.

The remarkable response of the ascites tumor cell to glucose addition consists of a momentary stimulation, followed by a considerable inhibition of respiration and glucose utilization. This observation of a latent high-respiratory activity of these cells suggests that metabolic control, and not irreversible damage (*3*), is responsible for their low respiratory activity under physiological conditions. Spectroscopic studies of effects coincident with the stimulation of respiration suggest that the control of respiration is being exerted at the level of the mitochondria by the glucose phosphorylating process and, reciprocally, that some property of the mitochondria is controlling the metabolism of glucose.

The Pasteur effect has previously focused attention upon glycolytic-respiratory activity interactions, as has the converse effect found by Crabtree (*15*). Much discussion of the role of phosphate and phosphate acceptor has appeared and has been incorporated in theories of metabolic control (*4–6*), especially by Belitzer (*7*), Johnson (*10*), Lynen and Koenigsberger (*11*), and Potter (*9*). Experimental data previously available to support these theories are largely based upon chemical analysis of extracts of intact cells such as yeast and, more recently, of the ascites tumor cells by Racker (*20*) and others. In these studies, the identification of the control substance in the ascites cell requires careful consideration. Lynen (*2*) and Racker (*20; 20a*) suggest that phosphate is of importance. Our spectroscopic and chemical studies of the ascites tumor cell indicate that increases and decreases of the intracellular concentration of adenosine diphosphate (ADP) are responsible for the changes of respiratory and glucose metabolism observed therein. This leads to the general view that a low intracellular concentration of ADP is responsible for the low rate of respiratory metabolism in these cells.

We present here a critical analysis of the components of the respiratory chain of the ascites cells and a study of the phosphorylation mechanism and its efficiency in isolated mitochondria, together with measurements of the above-mentioned responses of the intact cells to glucose addition.

Methods of Preparation

The preparations of ascites tumor cells and of mitochondria will be described in detail elsewhere (*21, 22*). It should suffice here to say that a six-day growth of tumor cells was used either directly suspended in the ascitic fluid or suspended in a "saline phosphate" solution (*21*) after differential centrifugation (and sometimes differential lysis) in order to free them from erythrocytes. The mitochondria were prepared by high-speed mechanical disintegration with subsequent differential centrifugation, a process which was developed for yeast granules (*23*). The reaction medium was that customarily used for the assay of oxidative phosphorylation (*24*), except that fluoride was omitted.

The chemical methods for assay of intermediates in the cells were mainly enzymatic reactions (*25*). Measurement of the activated phase of respiration of the cells requires a rapidly responding technique, and the vibrating platinum electrode was found to be excellently suited for this purpose (*26*).

The kinetics of spectroscopic changes were followed by a double-beam (two-monochromator) spectrophotometer (*13*), and difference spectra were plotted by a split-beam recording instrument (*13*).

Pathway of Electron Transfer in the Intact Cell

A method for determining the photochemical action spectrum for relief of carbon monoxide-inhibited respiration in the ascites tumor cell based upon the platinum microelectrode has shown clearly that cytochome a_3 is the terminal oxidase of this cell (*27*). Suggestions that the antimycin-A-insensitive pathway is of importance in certain tumor cells have been afforded by the work of Reif and Potter on the Flexner-Jobling carcinoma (*28*). This result would suggest that the respiratory pathway of the tumor cell would be largely a nonphosphorylating one. The report of the anomalous response of the succinate-oxidase pathway of the tumor cell (*29*) requires further investigation. In fact, the whole concept of "respiratory enzyme balance" (*30*) may be critically reevaluated.

Our investigation of the respiratory pathway is based upon the use of specific inhibitors: carbon monoxide for the terminal oxidase (*31*), antimycin A for the contribution of the cytochrome b_5 pathway (*24, 32*), and amytal for the relative importance of diphosphopyridine nucleotide and the succinate-linked mechanisms (*32–34*). The nature of the spectroscopic responses to these inhibitors also gives evidence for the sequence of cytochromes along the respiratory pathway.

Amytal almost completely blocks respiration of the ascites tumor cell: over 97 percent of the endogenous or glucose-activated respiration is inhibited by the addition of 2 mM amytal. The spectroscopic changes that accompany this inhibition correspond to a reduction of pyridine nucleotide and an oxidation of flavoprotein and cytochrome *b*. Thus the crossover point (*35*) for inhibition by amytal (its site of action) is between reduced pyridine nucleotide and flavoprotein. This is in agreement with the crossover point for amytal inhibition of isolated liver mitochondria (*34*), and suggests that this portion of the electron-transfer pathway of the intact ascites tumor cell is the same as that of isolated, actively phosphorylating mitochondria.

The fact that amytal treatment causes oxidation of the cytochrome components of the respiratory chain of the ascites cell that are largely reduced in the steady state of metabolism enables us to obtain a spectrum representing the difference between the fully oxidized and the fully reduced cytochrome components of the respiratory chain, as illustrated in Fig. 1. A comparison of the absorption bands of cytochromes *b*, *a* ($+a_3$), and $c+c_1$ with those of highly respiring cell suspensions such as baker's yeast (*36*) gives a qualitative idea of the normal balance of the components of the respiratory chain.

In the intact cells, antimycin-A treatment causes respiratory inhibition of

more than 95 percent. The titration of the cells with antimycin A clearly indicates that the reduction of cytochrome *b* proceeds after some nonspecific binding of antimycin A. Due to this nonspecific binding, the titration has a slope of roughly eight antimycin-A equivalents to one of cytochrome *b* (*21, 37*). The crossover point for antimycin-A inhibition is between cytochromes *b* and $c+c_1$, as would have been expected from studies of isolated mitochondria. It is interesting to note that no measurable shift of the α band of cytochrome *b* is caused by addition of antimycin A to the anaerobic tumor cell suspension, and thus the "modified cytochrome *b*" found in nonphosphorylating Keilin and Hartree preparations (*38*) is not present in these cells.

Spectroscopic studies of the absorbancy changes caused by dithionite addition to the anaerobic ascites tumor cell suspension suggest that no measurable amount of cytochrome b_5 is present in these cells. This is in accordance with the failure of attempts to isolate cytochrome b_5 from these suspensions (*39*).

The nearly complete inhibition of electron transfer in the intact cell by amytal and by antimycin A suggests that the electron-transfer pathway studied in isolated liver mitochondria (*40*) operates in the intact tumor cell. There is no evidence for the cytochrome b_5 or other antimycin-A-insensitive pathways for respiration of these cells. The abrupt and complete inhibition of respiration by amytal suggests that the pool of succinate in the ascites tumor cell is very small and that the respiratory pathway utilizes reduced pyridine nucleotide to a very great extent. The lack of respiratory stimulation upon addition of succinate to the amytal-treated cells is apparently due to their impermeability to this substrate rather than to a lack of succinate oxidase activity, and thus may provide an explanation of previous work (*29*).

Cytochromes of Whole Cells and of Mitochondria

A second method of studying the cytochrome content of the electron-transfer pathway of the cell is to isolate the mitochondria. The ascites tumor cells also afford an unusually favorable opportunity to compare the cytochromes of the whole cell with those of the mitochondria, since direct spectroscopic observations of both types of material are possible at room and liquid-air temperatures. A comparison of the "apparent absolute" spectra of substrate-reduced cytochromes of the azide-inhibited cells and their mitochondria is given in Fig. 2. The sharp absorption bands due to cytochromes *c*, c_1, *b*, and $a+a_3$-azide are clearly shown. All the components of the intact cells are present in the mitochondria. On the basis that the tightly bound cytochrome *a* has been retained in the mitochondria, we find that nearly all the cytochrome *c* of these cells is likewise retained by the mitochondria. Thus, speculation on respiratory pathways which depend upon the presence of cytochrome *c* in the cytoplasm, such as the cytochrome b_5 pathway, receives no support from these experiments. Dithionite treatment of the cells and their mitochondria show no specific absorbancy increases at low temperatures that could be attributed to cytochrome b_5, in confirmation of the results mentioned above.

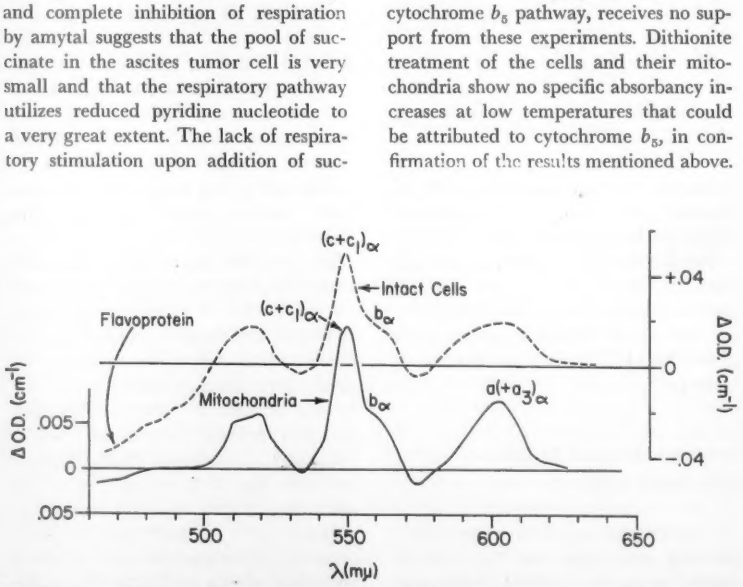


Fig. 1. Spectrum corresponding to absorbancy differences between the anaerobic ascites tumor cells and the aerobic cells treated with amytal in order to cause oxidation of the cytochrome components. In this difference spectrum, note that cytochrome *b* stands out clearly. For comparison, the difference spectrum of cytochrome components of the mitochondria isolated from the tumor cell is included. (Exp. 675e.)

There appears, however, a broad absorption band with a peak at approximately 560 mμ upon dithionite treatment of the enzymatically reduced material. This material does not appear to be a component of the respiratory chain and its possible identification with "mitochrome" (*41*) should not be overlooked.

Cytochrome Concentration: Respiratory Activity Relationships

On the basis of two types of spectrophotometric determinations of the cytochromes of the ascites tumor cells indicated by Figs. 1 and 2, we are now in a position to estimate any possible deficiency of cytochrome *c* and cytochrome oxidase in these tumor cells. Most of the previous conclusions have been based upon extraction procedures or enzymatic assays of solid tumors. It would appear that the direct determination of the respiratory components in intact cells and in isolated mitochondria of a homogenous population of freely suspended cells would have certain advantages over other procedures and other materials. In fact, a number of tumor cell suspensions derived from single clones (*42*) were placed at our disposal through the kindness of T. S. Hauschka (*43*). The results of assays of cytochromes of respiratory enzymes in ascites and other cells are given in Table 1. The relative amount of cytochromes appears to be independent of the ploidy. The amounts of the respiratory components computed relative to cytochrome *a* are typical of actively respiring cells, as indicated by comparison with yeast. Cytochrome *b* appears to be an exception, but the spectra are those corresponding to the transition from the aerobic steady state to the anaerobic state and therefore underestimate cytochrome *b* by a factor of about 3, as indicated by the studies with amytal and antimycin A. When this correction factor is applied, the content of cytochrome *b* much more nearly approaches that of other systems of highly active respiration. This type of correction is also necessary for evaluation of the total reduced pyridine nucleotide concentration.

In making up this table, the choice of materials has largely been set by their availability and suitability for the experimental method. The selection of yeast and muscle does not, therefore, represent our estimates of the "normal material" with which the ascites tumor cell should be compared, but instead represents selections of actively respir-

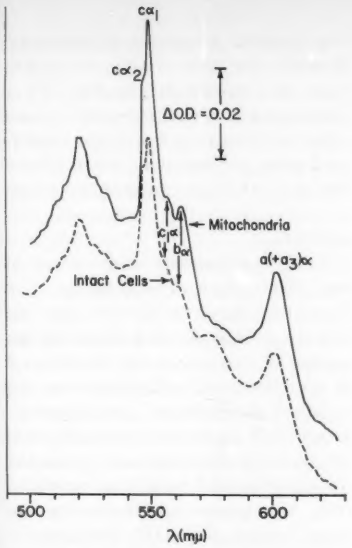


Fig. 2. Low temperature spectra of cytochrome components of intact cells and mitochondria isolated from them. These are "apparent" absolute spectra in which the reference material is the frozen solvent. The cytochrome components of the two types of material are appropriately designated. (Exp. 675e.)

ing electron-transfer systems on which data are available.

When cytochrome concentration is calculated on a weight basis instead of on a relative basis, it is seen that the ascites cells lie between baker's yeast and frog muscle. On this basis, it is apparent that the cells have not only an appropriately proportioned cytochrome system, but also a relative sufficiency of these enzymes in the cell. An examination of the mitochondria prepared from the ascites tumor cells shows that the cytochrome content per milligram protein is very nearly the same for the three types of materials assayed here. This leads to the noteworthy conclusion that mitochondria derived from these three different sources have essentially the same constitution, with the exception of the values for reduced pyridine nucleotide, which will vary somewhat because of the variable loss of reduced pyridine nucleotide in the preparation of mitochondria.

Of greatest interest are the data on the turnover number of cytochromes, especially those comparing the turnover number of cytochromes in the intact cell and in the isolated mitochondria. It is clear that the turnover number of cytochrome *a* in the intact cell is low with respect to both that of its isolated mitochondria and that of other types of cells. For example, mitochondria isolated from ascites cells have the same turnover number as mitochondria isolated from rat liver (10 sec^{-1}) (*24*), but cytochrome *a* in the intact cell turns over at only 3 sec^{-1}. This leads to the conclusion that while the concentration of cytochrome in the intact cell is adequate, the respiratory system is not used to the extent of its capabilities. This result independently suggests that, instead of an "unbalanced" enzyme system, there is a control mechanism imposed upon the respiratory activity of the intact ascites tumor cell.

Properties of Mitochondria Prepared from Ascites Tumor Cells

A key point in any consideration of metabolic control by the mitochondria is a determination of whether their electron transfer can actually be controlled by the concentration of phosphate and phosphate acceptor, as has been demonstrated for mitochondria isolated from liver by Lardy and Wellman (*44*) but not for mitochondria from ascites cells (*45*). Although the preparation procedure requires vigorous shaking with glass beads to rupture the cell, it has been possible to demonstrate respiratory control in these mitochondria. We find respiratory control ratios to average threefold and to exceed sixfold with succinate as substrate. The average P/O value with succinate as substrate is 1.8, as compared with previous values of 1.4 (*43*). Thus these mitochondria show good respiratory control and phosphorylation efficiency. The high phosphorylation efficiency of ascites mitochondria is suggested by indirect data of Quastel and Bickris (*46*).

A further finding of studies of the effect of ADP upon the isolated mitochondria is their spectroscopic response, illustrated by Fig. 3. Here, addition of ADP to the substrate-treated mitochondria (state 4) causes a disappearance of the absorption bands of reduced pyridine nucleotide, flavoprotein, cytochrome *b*, and cytochrome *c* (see *35*). (The decreases of absorbancy are plotted as an upward deflection in order to aid in the recognition of the absorption bands.) For comparison, the difference spectra corresponding to those absorption bands which appear in anaerobiosis are included.

In summary, experimental results show that respiration of mitochondria isolated from ascites tumor cells can be readily activated by adding ADP. Furthermore, characteristic spectroscopic changes are observed which could be used to identify changes of ADP concentration within the intact cells.

Respiratory Response to Glucose

A response similar to that of the isolated mitochondria to the addition of ADP is found under certain conditions with the intact cells. As indicated above, it is clear that the respiratory activity proceeds at a low rate under endogenous

Table 1. Respiratory components of cells and mitochondria.

Material	Designation	Chromosome No.	Cytochrome *a*		Relative amounts of respiratory enzymes						
			Amount	Turnover No. (sec^{-1})	a	b	$c + c_1$	fp	a_3	RPN	Expts.
Ascites cells	E L stock	46	7*	3	1	0.3†	2.2	4.4	0.9	6†	225
Ascites cells	E-1	84	9*	3	1	0.4†	2.6	3.5		6†	232
Yeast cells	"Bakers"		20*	52	1	1.4	2.5	1.5	1.6	6	911
Excised muscle	Frog sartorius		2*		1	0.6†	1.8	3	0.8	20†	W-1
Mitochondria	Ascites cells (E L stock)		2‡	10§	1	1	3.1			10	662
Mitochondria	Rat liver		2‡	9§	1	0.9	1.7	3.6		19	

* Units: moles/g cells × 10^9. † Steady-state oxidized only; considerably more of the component is present. ‡ Units: moles/mg pr × 10^{10}. § Glutamate as substrate.

metabolism and that the mitochondria have a capability of at least a threefold acceleration over this rate. Addition of glucose to a suspension of the intact cells freshly drawn from the mouse and suspended in the ascitic fluid or in the saline phosphate medium shows a rapid acceleration of respiration (Fig. 4), varying from two- to sixfold and depending largely upon the nature of the endogenous metabolism.

A second respiratory response is indicated by Fig. 4. It shows that after approximately a minute of accelerated respiration, a severe inhibition sets in which reduces the respiratory rate below that previously obtained with endogenous substrate. The record further shows that this inhibited respiration is largely relieved by the addition of an uncoupling agent such as dicoumerol (Fig. 4*A*) or dinitrophenol (Fig. 4*B*). The amount of oxygen taken up during the accelerated phase of respiratory metabolism in the presence of excess glucose is linearly related to the number of cells used (*47*).

Some pertinent data on the nature of this effect follow. The acceleration of respiration does not depend upon the activity of the Embden-Meyerhof sequence of enzymes; it can be obtained in the presence of sufficient iodoacetate to inhibit the glycolysis. Thus the acceleration does not depend upon additional substrate for the respiratory chain, but instead upon an intermediate produced from the glucose-phosphorylating enzymes—presumably ADP. This observation further suggests that the inhibition of the glucose-activated respiration is due to a depletion of the intracellular store of adenosine triphosphate (ATP) available to the glucose-phosphorylating enzymes. Furthermore, the inhibition of respiration does not depend upon the expenditure of ADP by phosphoglycerate kinase, not only because of the relatively higher affinity of the mitochondria for ADP but also because the inhibition is observed in the presence of iodoacetate.

Further evidence for the cause of the inhibition is provided by the fact that the addition of an amount of glucose smaller than the intracellular store results, nevertheless, in respiratory inhibition after a brief interval of oxygen uptake (Fig. 4*C*). Respiration may be started again by a second addition of glucose. In this case, the same intracellular store is depleted, for the total oxygen uptake due to the two additions of glucose is equal to that caused by the addition of one large excess of glucose. This reactivation of respiration by a further addition of glucose is of considerable significance in interpreting the control mechanism. Since ADP from the glucose-phosphorylating enzymes is the logical cause of the reactivation of respiration, it may be concluded that lack of ADP is the cause of the inhibition. It is further reasonable to conclude that when respiration is blocked about a minute after addition of an excess of glucose, lack of ADP is also the cause. Thus, increases and decreases of the intracellular concentration of ADP appear to be responsible for the increases and decreases of the respiratory rate caused by glucose addition.

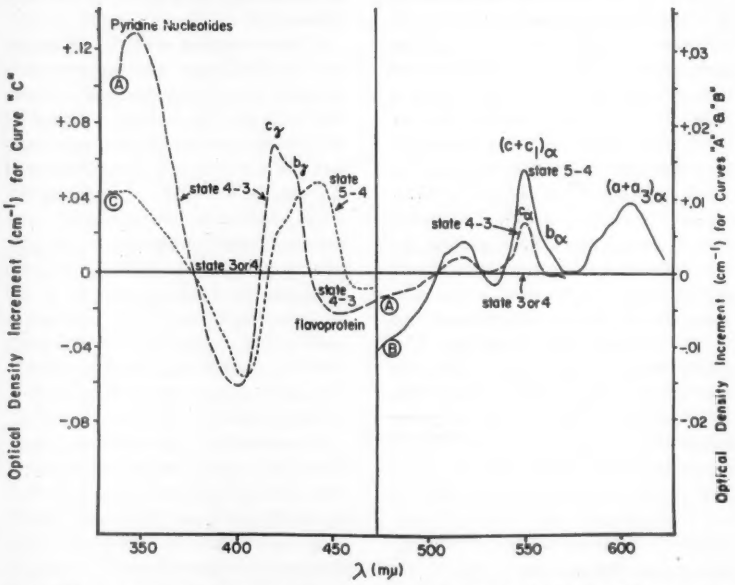


Fig. 3. The spectroscopic response of a suspension of mitochondria isolated from ascites tumor cells to an exhaustion of added ADP (trace A state 4–3 transition). Upon exhaustion of added ADP, absorption bands appear corresponding to the reduction of the pyridine nucleotides, flavoprotein, and cytochromes *b* and *c*. For comparison, the absorption changes that occur when the aerobic mitochondria become anaerobic are included (traces B and C, state 5–4). (Exp. 662d-3.)

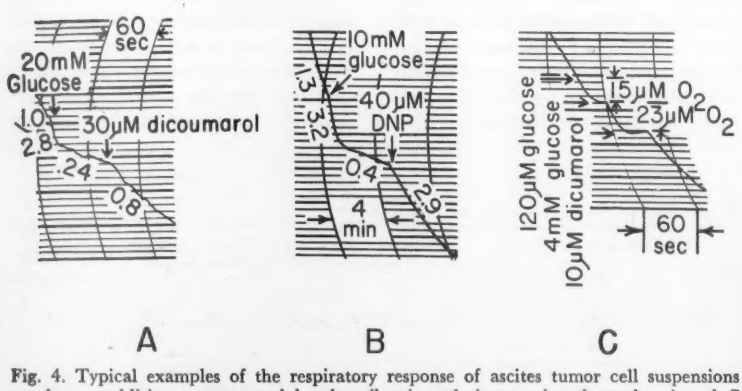


Fig. 4. Typical examples of the respiratory response of ascites tumor cell suspensions to glucose addition as measured by the vibrating platinum microelectrode. *A* and *B* represent the acceleration and inhibition of endogenous respiration of ascites tumor cell suspensions caused by the addition of glucose together with the restarting of this inhibited respiration by the addition of uncoupling agents (dicoumarol, *A*; dinitrophenol, *B*). In *C*, a rather low concentration of glucose (120 μ*M*) is added, which soon leads to an inhibition of respiration. The addition of an excess of glucose restarts the respiration, which again is inhibited after a short period. Respiration may be further restarted by addition of dicoumarol. (Exps. 647e, 677a.)

Spectroscopic Response to Glucose

The preceding data suggest an ADP control of metabolism in the intact ascites tumor cell, and an incisive confirmation of this can be obtained from studies of the spectroscopic response of the mitochondria of the intact cell to the addition of glucose. One of the clearer records of this phenomenon is indicated by Fig. 5, in which both respiratory and spectrophotometric methods are shown in the top two traces. The former record shows the usual phenomenon of acceleration and inhibition of respiration about a minute after adding glucose. The spectroscopic trace shows an abrupt upward deflection corresponding to an oxidation of cytochrome *b* which persists during the activated phase of respiration and subsides as the respiratory activity subsides. This would appear to be the characteristic response of the respiratory chain to an increase of ADP concentration produced during the phosphorylation of glucose (see Fig. 3 at 430 mμ).

Two of the cytochrome components affected by glucose addition are suggested by studies of the difference spectrum obtained with a rapidly recording split-beam spectrophotometer. It is found that glucose addition causes the fused Soret bands of both cytochromes *b* and *c* to diminish in intensity. Studies similar to those of Fig. 5 verify that these absorbancy changes also occur in the visible region of the spectrum (562 and 550 mμ). In summary, reduced pyridine nucleotide, flavoprotein, cytochromes *b* and *c*, and in some cases cytochrome *a* are more oxidized during the glucose-activated phase of respiration.

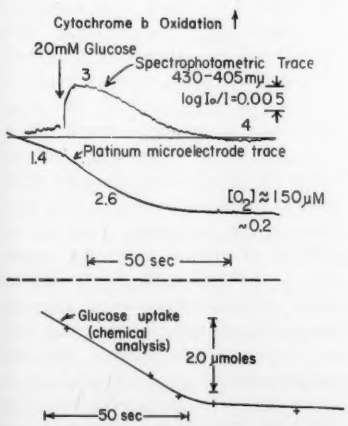


Fig. 5. Spectroscopic response accompanying acceleration and inhibition of respiration caused by glucose addition to a suspension of ascites tumor cells. The spectrophotometric trace is recorded with the double-beam spectrophotometer at 430 mμ (405 mμ as a reference). (The changes of respiratory rate are measured by the platinum microelectrode.) In a separate experiment, with a different suspension of ascites tumor cells, chemical analysis shows glucose uptake to proceed rapidly following the addition of glucose and to be inhibited about a minute after its addition. (Exp. 498b, 0-92.)

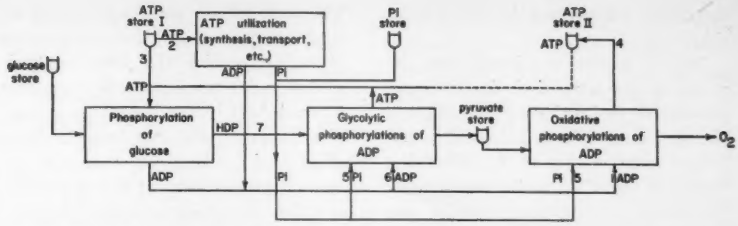


Fig. 6. Possibilities for metabolic control in ascites tumor cells: a schematic representation of interaction of glucose phosphorylating enzymes, glycolytic phosphorylations of ADP, and oxidative phosphorylations of ADP. In the interests of simplicity, many other interactions are arbitrarily omitted. The numbers refer to points at which control of metabolism may be exerted as follows: (1) Control of respiration by ADP concentration. (2) Control of ATP utilization by endogenous processes by the ATP concentration. (3) Control of the rate of glucose phosphorylation (either hexokinase or phosphohexokinase) by the ATP level. (4) A reservoir in which ATP formed in mitochondrial oxidative phosphorylation may be retained in such a way that it is not readily available for glucose phosphorylation. (5) Control of glycolytic or oxidative phosphorylation by the inorganic phosphate level. (6) Control of glycolytic phosphorylation by the ADP level. (7) Control of glycolytic phosphorylation by the substrate level (hexosediphosphate). (MD-65.)

These data identify a crossover point (*35*) above cytochrome *c* for the activation of the respiratory chain of the ascites tumor cell caused by glucose addition. This is in agreement with the experiments on isolated mitochondria where the same components were observed to be oxidized on ADP addition. In combination with the data of Fig. 4, we put forward strong evidence for the supposition that ADP produced in phosphorylation of glucose momentarily activates the mitochondria of the cell and allows these slowly respiring cells to show their latent respiratory activity.

Regulation of Metabolism

Some responses of the cell to a change of its environment involve metabolic regulations. A well-known example of such a response is the Pasteur effect, in which the change in environment may be from oxygen to nitrogen, and vice versa. The metabolic responses to these changes are manifestations of the underlying mechanisms. Some responses may give incisive information about the mechanism, others may not. The Pasteur response has been studied in detail for many years, but the lack of definitive results suggests that the consequences of initiation or cessation of oxygen metabolism are manifold and not easy to interpret. Initiation of glucose metabolism involving the Crabtree response appears to be more easily understood, and two new responses, described below, are found most useful in the study of mechanisms of metabolic control. Ascites tumor cell suspensions are found to give four types of responses, two of which clearly differ from the Pasteur and Crabtree effects; the third has a feature in addition to the Crabtree effect; and the fourth is a type of Pasteur reaction. These responses have been studied in detail in order to reveal the steps in the reaction mechanism that can control metabolism.

The sequences of chemical reactions involved in glucose and oxygen metabolism of the ascites tumor cell are schematically represented from the standpoint of possible pathways of metabolic control in Fig. 6. The Embden-Meyerhof sequence of glycolytic reactions is divided into two parts, "phosphorylations of glucose" and "glycolytic phosphorylations of ADP," to emphasize ATP utilization and synthesis. The Krebs cycle and the respiratory chain are lumped together as "oxidative phosphorylation of ADP" to emphasize ATP synthesis by these enzymes. The hexosemonophosphate shunt is not included because it does not exert a direct effect upon the ATP level, and TPNH formed in this pathway is not an essential intermediate in these regulations. The utilization of ATP by the cell for synthesis, transport, and other functions is indicated as a single function. Reserves of ATP, pyruvate, and glucose are relevant to the discussion that follows; other

substances are omitted for the sake of simplicity.

In cells freshly withdrawn from the mouse at about the sixth day of tumor growth, we find an endogenous respiration that is not greatly increased by pyruvate addition. Figure 6 indicates a "pyruvate store" in which are lumped the Krebs cycle substrates which are apparently in excess in the endogenous condition. Glucose is present in low concentrations. ATP is accumulated in a store available to hexokinase.

The first response to glucose addition is an activation of glucose phosphorylation, and the ADP formed thereby activates respiration (line 1, Fig. 6). In terms of the responses of isolated mitochondria to ADP addition, the state 4–3 transition occurs (*35*).

The second response occurs where the added glucose concentration is less than the store of ATP and consists of an inhibition of endogenous respiration after the added glucose has been expended in phosphorylation reactions. The excess ADP formed during glucose phosphorylation is also expended by the mitochondria, and respiration slackens because of lack of ADP—a typical state 3–4 transition in terms of the response of isolated mitochondria to a decrease of ADP concentration. The most striking feature of this second response is the decrease of respiratory rate to a level considerably below that characteristic of endogenous metabolism (see Fig. 4*C*).

A possible explanation for this inhibition is that the ATP utilization associated with endogenous metabolism has a low ATP affinity and a small decrease of the ATP store I (Fig. 6) is inhibitory. For example, the utilization of acetate has clearly been shown to be sensitive to dinitrophenol (*48*), and although it is not possible to identify the ATP-utilizing reactions involved here, a sensitivity to the ATP concentration is not unexpected.

The third response occurs in the presence of an excess of glucose and consists of an inhibition of both glucose utilization and respiration. In this case, the first response lasts longer, and accelerated respiration and glucose utilization continue for about a minute, depending upon the condition of the cells, that is, upon the amount of their ATP in store I (Fig. 6). When this ATP store has been expended, respiration and glucose utilization decrease very markedly (see Fig. 5). A slackening of respiration after glucose addition has been observed in long-term experiments by Crabtree (*15*). The very intense, short-term effects recorded here are clearly due to a lowering of the intracellular ADP level that leads to a state 3–4 transition and to a system in which ADP is rate-limiting for respiration. However, the long-term Crabtree effect need not be a consequence of the same metabolic control; it is not necessary that all metabolic controls be exercised by the same chemical.

The slackening of glucose metabolism in the presence of excess glucose (bottom trace, Fig. 5) is a novel part of the third response and requires special consideration. The above-mentioned reduction of the ATP store is unexpected because the ADP formed in glucose phosphorylation is largely rephosphorylated at ATP in the mitochondria (top trace, Fig. 5, and line 4, Fig. 6). The simplest hypothesis is that the ATP formed in the mitochondria is not directly available for glucose phosphorylation. It would appear that a compartment (see Lynen and Koenigsberger, *11*; see also *16, 21, 49*) or an equivalent system for the retention of this newly formed ATP (line 4, Fig. 6) may interrupt the flow of ATP back to the glucose-phosphorylating enzymes and thereby control glucose utilization. The unavailability of the ATP to glucose phosphorylation is apparently subject to change with time; we find that the inhibition diminishes (see also *20a, 50*) and that uncoupling agents abolish the inhibition as discussed below.

A fourth response is the release of inhibition of respiration and of glucose utilization by the addition of an uncoupling agent. Figures 4*A* and 4*B* clearly illustrate the reversal of respiratory inhibition, and separate chemical studies, similar to those of Fig. 5 (see *25*; see also *20, 20a*), show the activation of glucose utilization. The explanation of the respiratory effect is straightforward: the mitochondria no longer require ADP (or phosphate) for respiration in the presence of an uncoupling agent (lines 1 and 5 of Fig. 6 are not needed). The effect upon glucose utilization is a typical Pasteur response (rapid aerobic glycolysis in the presence of various uncoupling agents). A hypothesis that is consistent with an explanation of the three responses described above is that a redistribution of ATP occurs upon addition of the uncoupling agent. In this redistribution, more ATP becomes available for the phosphorylation of glucose and more ADP (and phosphate) becomes available to the glycolytic phosphorylations (see *11*).

While these four responses of the schematic representation of Fig. 6 are given here in qualitative terms, a complete representation of the kinetics of 26 chemical components in 17 equations has been accomplished by means of a special chemical kinetics program for Univac I (*51, 52*). These solutions, which will be discussed in detail elsewhere (*53*), show a quantitative correspondence to the four responses observed experimentally. Thus, the three features of this hypothesis—(i) an overriding ADP affinity at the mitochondria (*8–10, 26, 54*) which are under control of the ADP level (*44*), (ii) a compartmentalization (*11*) of newly phosphorylated ATP (*16*) which can be released by uncoupling agents or by anaerobiosis (*11, 20*), and (iii) a sensitivity of ATP utilization to the intracellular ATP level—appear to be adequate for an over-all description of our currently available experimental data. The agreement of the computer solutions and the experimental data does not of itself eliminate other hypotheses for metabolic control, and they are discussed below.

The possibility of a control of the activity of phosphohexokinase has been suggested from time to time. Recently Aisenberg and Potter have suggested that mitochondria exert this control (*55*), and their conclusion would appear to be applicable to the studies reported by Lynen (*2*). While it is apparently true that liver mitochondria, when mixed with the supernatant fluid from a brain homogenate, exert an inhibitory influence on glycolysis (*55*), the direct experiment on the ascites tumor cell indicates that the relationship of this enzyme to the mitochondria under physiological conditions is such that an inhibition is not noticeable. Prior to the addition of glucose under the experimental conditions in Fig. 5, the cells are in an excellent physiological state for the postulated inhibition to apply; they are respiring fairly actively, thus the concentration of any inhibitor (such as Y-phosphate) would be expected to be high (*55*). Nevertheless, added glucose is rapidly utilized in direct contradiction to the proposed inhibition mechanism. This experimental observation also makes it unlikely that the accumulation of glucose-6-phosphate is a cause of the inhibition of respiration, since, in this case, the second addition of glucose (Fig. 4*C*) would not accelerate respiration to the same extent as the first addition. Thus the explanation of ATP retention after its phosphorylation by the mitochondria, together with the decrease

of ATP available to hexokinase, is a hypothesis that is presently in agreement with the experimental data on the whole cell.

Ibsen, Coe, and McKee (*20a*) propose that Seikevitz and Potter's (*56*) hypothesis for ATP-AMP control of respiration applies here. However, the isolated mitochondria from the ascites tumor cell respond rapidly and directly to ADP alone, and liver mitochondria respond five times more rapidly to ADP than to AMP (*57*). In addition, the chemical data (*20a*) show responses of ADP that are much more appropriate to metabolic control by ADP than by AMP (see Fig. 8 in *20a*).

Chemical analysis of the changes of ATP and ADP during the first and third responses are in good qualitative agreement with the mechanism described (*20a, 25*). In the phase of activated metabolism the ATP level falls and the ADP level rises, and vice versa in the inhibited phase of metabolism. Phosphate falls somewhat in the activated phase due to the phosphorylative activity, but rises somewhat in the inhibited phase, in agreement with our conclusion that lack of phosphate does not control the respiratory rate at this time (*47*).

In the inhibited state of respiration after the third response, the levels of ATP, ADP, and inorganic phosphate as analyzed after disruption of the cell show average concentrations which are all in excess of the Michaelis constants for glucose phosphorylation or for respiration. Lynen (*2*) finds a related paradox in his chemical studies of the Pasteur effect in yeast cells. The response of the intracellular hexose phosphates to increased oxygen clearly indicates metabolic control in the glucose-phosphorylating enzymes, probably due to a decrease of ATP concentration, yet the chemical data show no measurable change of the average ATP concentration. Furthermore, chemical analyses of muscle in the resting state give results that are obviously inconsistent; the average ADP and phosphate levels are sufficient to give maximal respiratory activity (*58*), but the mitochondria are shown by spectroscopic observations of the respiratory carriers to be substantially free of phosphate or phosphate acceptor (*59*). It would appear, therefore, that chemical analysis without intracellular localization can at best be only suggestive of the concentration of a rate-limiting component and cannot be used to appraise metabolic responses involving a redistribution of nucleotides.

There have been two recent attempts to reconstruct the interactions indicated by Fig. 6 by mixtures of enzymes and mitochondria (*55, 60*). Such systems can be arranged to be dependent upon any one of the lines that interconnect the functions of Fig. 6 and are most useful for a demonstration of these properties of the system. However, two or more properties of the intact cell may be lacking. First, the retention of newly phosphorylated ATP may not occur; and second, the control of respiration in the mitochondria by the phosphate and phosphate acceptor level is a very labile effect which may be impaired by the conditions of the experiment. The remaining metabolic controls would be due to phosphate or phosphate acceptor at the level of substrate phosphorylations or to the substrate concentration itself at any point in the system. The fact that Wu and Racker (*60*) find inorganic phosphate (line 5, Fig. 6) and Aisenberg and Potter (*55*) find hexose diphosphate (line 7, Fig. 6) to be controlling under certain conditions in the reconstituted system is not unexpected.

In different types of intact cells, the integrated action of the components of the system of Fig. 6 may not be expected to involve identical controls. Yeast and ascites tumor cells which have been studied by these methods demonstrate quantitatively different responses. In yeast, respiratory changes attributable to the retention of ATP can readily be demonstrated, but are less marked, probably because the energy utilization by endogenous processes is less sensitive to changes in the ATP concentration. It is also possible that the control which ADP can exert over electron transfer in the mitochondria of the intact yeast cell is less marked than in mammalian cells, since isolation of yeast mitochondria in a state that demonstrates respiratory control has not yet been accomplished. In microorganisms, evidence for respiratory control in isolated mitochondria is also lacking. However, the Pasteur effect, for example, does not require a universal mechanism; cells without mitochondrial respiratory control would show aerobic inhibition of glucose uptake simply by retention of ATP (see Fig. 6). Such cells would not be expected to show a Crabtree effect, and so far this effect is found only in tumor cells. On the other hand such cells might employ the alternative pathways for metabolic control indicated by Fig. 6.

Since the mitochondria cannot be used as indicators of the ADP and phosphate levels in the anaerobic cell, this experimental approach affords no new information under these conditions, and anaerobic glycolysis may be controlled by the alternate pathways of Fig. 6.

Summary

The Pasteur and Crabtree effects demonstrate that changes at the beginning of the metabolic sequence for glucose metabolism give rise to effects at the end, and vice versa. We have presented here three additional responses of the ascites tumor cell suspensions, and presumably more will be uncovered. Each one of these responses is a manifestation of factors in the underlying mechanism that are in the nature of chemical feedback of a linear or nonlinear nature. The metabolic reactions are sufficiently complex that it is unlikely that any single component or step need control metabolism in different types of cells or under all conditions for a particular cell. However, it is due to a favorable circumstance that, in an appropriate type of cell and with the use of a direct intracellular indicator for changes in ADP concentration, we can state that the respiratory metabolism of the ascites tumor cell suspension, as freshly withdrawn from the mouse abdomen, is limited by the intracellular ADP concentration, and that this is why these cells show a predominance of glycolytic over respiratory activity. The response of the metabolism to small and large additions of glucose illustrates aspects of the metabolic mechanism which involve control of endogenous metabolism and compartmentalization of ATP formed in oxidative phosphorylation, the net result being a depression of the respiratory activity. The results of this approach emphasize the importance of chemical assays of localized portions of the living cell in its physiological state (*61*).

References

1. T. K. Walker, *Nature* **181**, 940 (1958).
2. F. Lynen, in *Neuere Ergebnisse aus Chemie und Stoffwechsel der Kohlenhydrate* (Springer, Berlin, 1958), p. 155; summarized in *Proceedings of the International Enzyme Symposium, Tokyo, October 1957* (Academic Press, New York, 1958).
3. O. Warburg, *Science* **123**, 309 (1956).
4. W. A. Engelhardt, *Biochem. Z.* **251**, 343 (1932).
5. A. Lennerstrand, *Biochem. Z.* **289**, 104 (1937).
6. ———, *Naturwissenschaften* **25**, 347 (1937).
7. V. A. Belitzer, *Enzymologia* **6**, 1 (1939).
8. F. Lynen, *Ann. Chem. Liebigs* **546**, 120 (1941).
9. V. R. Potter, *Advances in Enzymol.* **4**, 201 (1944).
10. M. J. Johnson, *Science* **94**, 200 (1941).
11. F. Lynen and R. Koenigsberger, *Ann. Chem. Liebigs* **573**, 60 (1951).

12. R. A. Peters, *Nature* 177, 426 (1956).
13. B. Chance, *Science* 120, 767 (1954).
14. R. W. Miner, *Ann. N.Y. Acad. Sci.* 63, 637 (1956).
15. H. G. Crabtree, *Biochem. J.* 23, 536 (1929).
16. B. Chance and B. Hess, *Ann. N.Y. Acad. Sci.* 63, 1008 (1956).
17. O. Warburg and W. Christian, *Biochem. Z.* 314, 399 (1943).
18. J. P. Greenstein, *Cancer Research* 16, 641 (1956).
19. B. Chance and L. N. Castor, *Science* 116, 200 (1952).
20. E. F. Racker, *Ann. N.Y. Acad. Sci.* 63, 1017 (1956).
20a. H. K. Ibsen, E. L. Coe, R. W. McKee, *Biochim. et Biophys. Acta* 30, 384 (1958).
21. B. Chance and B. Hess, "Electron transfer in the mammalian cell," in preparation.
22. ———, "Crossover phenomena in mitochrondria of the ascites tumor cell," in preparation.
23. P. M. Nossal, *Australian J. Exptl. Biol. Med. Sci.* 31, 583 (1953).
24. B. Chance and G. R. Williams, *J. Biol. Chem.* 217, 395 (1955).
25. B. Hess and B. Chance, "Chemical events following addition of glucose to ascites tumor cells," in preparation.
26. B. Chance and G. R. Williams, *J. Biol. Chem.* 217, 383 (1955).
27. L. N. Castor and B. Chance, *ibid.* 217, 453 (1955).
28. A. E. Reif and V. R. Potter, *Cancer Research* 13, 49 (1953).
29. J. G. Kidd, R. J. Winzler, D. Burk, *ibid.* 4, 547 (1944).
30. V. R. Potter, *ibid.* 16, 658 (1956).
31. O. Warburg and E. Negelein, *Biochem. Z.* 214, 64 (1929).
32. B. Chance, in *Methods in Enzymology*, S. P. Colowick and N. O. Kaplan, Eds. (Academic Press, New York, 1957), vol. 4, p. 273.
33. L. Ernster, O. Jalling, H. Löw, O. Lindberg, *Exptl. Cell Research* Suppl. 3, 124 (1955).
34. B. Chance, in *Enzymes: Units of Biological Structure and Function*, O. H. Gaebler, Ed. (Academic Press, New York, 1956), p. 447.
35. ——— and G. R. Williams, *Advances in Enzymol.* 17, 65 (1956).
36. B. Chance, in *The Mechanism of Enzyme Action*, W. D. McElroy and B. Glass, Eds. (Johns Hopkins Press, Baltimore, 1954), p. 399.
37. ———, *Nature* 169, 215 (1952).
38. ———, *J. Biol. Chem.* 233, 1223 (1958).
39. D. Garfinkel, in preparation.
40. B. Chance and G. R. Williams, *J. Biol. Chem.* 217, 429 (1955).
41. D. B. Polis and H. W. Schmuckler, *Abstr. Am. Chem. Soc. Meeting, New York, Sept. 1954*, 126, 72C.
42. K. Kaziwara, *Cancer Research* 14, 795 (1954).
43. T. S. Hauschka, S. T. Grinell, L. Révész, G. Klein, *J. Natl. Cancer Inst.* 19, 13 (1957).
44. H. A. Lardy and H. Wellman, *J. Biol. Chem.* 195, 215 (1952).
45. O. Lindberg, M. Ljunggren, L. Ernster, L. Révész, *Exptl. Cell Research* 4, 243 (1953).
46. J. H. Quastel and I. J. Bickris, *Nature* 183, 281 (1959).
47. B. Hess and B. Chance, "Phosphorylation efficiency of the intact cell. I. Glucose-oxygen titrations in ascites tumor cells," in preparation.
48. A. C. Aisenberg and V. R. Potter, *J. Biol. Chem.* 215, 737 (1955).
49. H. Holzer, J. Witt, R. Freytag-Hilf, *Biochem. Z.* 329, 467 (1958).
50. E. Coe, K. Ibsen, R. W. McKee, *Federation Proc.* 17, 203 (1958).
51. B. Chance, in *Proceedings of the Ciba Foundation Symposium on the Regulation of Cell Metabolism* (Churchill, London, in press).
52. D. Garfinkel, J. Higgins, J. D. Rutledge, "A digital computer program for the study of chemical kinetics," in preparation.
53. B. Chance, D. Garfinkel, J. Higgins, "A minimum hypothesis for the dynamics of interactions between glycolysis and respiration in ascites tumor cells," in preparation.
54. E. Slater and F. A. Holton, *Biochem. J.* 55, 530 (1953).
55. A. C. Aisenberg and V. R. Potter, *J. Biol. Chem.* 224, 1115 (1957).
56. P. Siekevitz and V. R. Potter, *ibid.* 215, 237 (1955).
57. B. Chance, *ibid.* 226, 595 (1957).
58. A. Fleckenstein, J. Janke, R. E. Davies, H. A. Krebs, *Nature* 174, 1081 (1954).
59. B. Chance and C. M. Connelly, *Nature* 179, 1235 (1957).
60. R. Wu and E. Racker, *Federation Proc.* 16, 274 (1957).
61. This research was supported in its later phases by a grant from the American Cancer Society.

News of Science

Science Advisory Committee's Recommendation for Science Council Being Implemented by Executive Order

Rapid progress is being made on the implementation of the proposal of the President's Science Advisory Committee for the establishment of a Federal Council for Science and Technology. Informed observers in Washington indicate that an executive order establishing the new council and giving its membership can be expected very soon. The interagency council will have responsibility for promoting coordinated science policy planning and more effective management of federal programs in science and technology. The recommendation for the council was made last December in the report "Strengthening American Science" issued by the President's Science Advisory Committee.

Major Problems Solved

At this writing, the executive order that will bring the council into existence is being reviewed by the Justice Department for any legal or jurisdictional problems that might have been overlooked by its framers in the executive department. Customarily, this review is the last step before an executive order is signed. Both the quality of the Advisory Committee's original report and the early solution of the thorny problem of council membership have contributed to the rapid progress of the work, according to various governmental sources. The membership problem offered one of the greatest difficulties. How many of the governmental agencies doing scientific work should be represented on the council? The committee report called for a membership of nine persons —the chairman and eight representatives from the various major governmental agencies doing scientific and technological work.

The agencies, which were selected primarily on the basis of their expenditures for scientific activity, were the National Science Foundation, the Atomic Energy Commission, the National Aeronautics and Space Administration, and the departments of Defense, Interior, Commerce, Agriculture, and Health, Education, and Welfare. The committee's recommendation was accepted, and representatives of these agencies will constitute the council. In the case of three agencies, the National Science Foundation, the Department of Defense, and NASA, the representatives are known. In order, they are Alan Waterman, Herbert York, and T. Keith Glennan. All but two of the remaining representatives are said to have been decided upon. It is expected that these persons will not be given new positions in their departments, but rather, they will be the existing secretary, one of the assistant secretaries, or a special assistant. In all cases the object is to have one man with general policy responsibility to represent effectively all the technical activities of his department. The position of Director of Defense Research and Engineering in the Defense Department exemplifies the type of representation the council needs. This position, now held by Herbert York, was defined recently by Secretary McElroy as the top research and development position in the Department of Defense.

A second problem that has been treated successfully by the Bureau of the Budget personnel working on the executive order is that of reconciliation of previous executive acts with the new one. Orders which gave the National Science Foundation authority to coordinate governmental scientific activity and which established the Interdepartmental

Committee on Scientific Research and Development have been reviewed to ensure that they are consonant with the responsibilities of the new council. This reconciliation, with its time-consuming legal and jurisdictional complexities, was the major procedural problem faced by those concerned with the order, it is understood.

Few Changes Made

The executive order is expected to follow the outline of the committee report on all major points. One of the few deviations is said to be that giving a greater emphasis to international aspects of science planning. It is believed that the recommendation that the science adviser to the Secretary of State attend the council's meetings as an observer will be supplemented by other provisions that will promote greater recognition of the world-wide scope of American scientific efforts.

The Science Advisory Committee's report states that "the chairman of the council should be the Special Assistant to the President for Science and Technology." There is every reason to believe that this recommendation will be accepted and that the first council president will be James R. Killian.

Indirect Effects of Council Planning

One effect of the work of implementing and staffing the Federal Council for Science and Technology was to stimulate thinking among the various federal agencies doing scientific work. When officials of the Bureau of the Budget asked for recommendations of persons to sit on the council the agencies whose scientific activities are fragmented and dispersed were forced to examine their organizations and personnel. They had to ask themselves if they each had a man who was sufficiently on top of all the agency's scientific activity that he could speak for it before the council. When such men could not be found, it is reported, duties were assigned and staff work was begun that would fill the need. This is one of the things the Science Advisory Committee's report was designed to accomplish.

Opportunities of the Council

Great hopes are entertained by the committee for the new council. It is viewed as a means of eliminating the many *ad hoc* groups that have from time to time attempted to effect some coherent planning of the Government's vast scientific activities and replacing them with one group with direct access to the executive department and with sufficient authority to reconcile the many programs that are put forth by the various agencies. Clear alternatives could be presented to the President, and the "capital and manpower bind" that now adversely affects many projected scientific programs could be resolved in the way that best serves the national interest.

Relationship to a Department of Science

Contrary to some speculation, the new council is not to be viewed as a prototype for an eventual department of science, according to informed sources. It is simply an attempt to solve the programming, funding, and resources problems that have multiplied to an unmanageable degree since the end of World War II. Science has come to be a major element in the national welfare and the national defense; the advisory committee believed that a Federal Council for Science and Technology offered the best means to accomplish this end. It was devised and offered to solve particular problems in the most efficient way, and not to set the stage for a department of science or to abort any efforts in that direction. In the view of one commentator, one of the great virtues of the council is that it is an innovation without the status and inertia of a full-fledged department. If it works, if it solves the specific problems to which it is addressed, so much to the good. If it does not, it can be abolished and replaced by whatever its experience shows to be the better mechanism—perhaps a department of science. But the view here is that the Federal Council for Science and Technology has the background planning, the cooperation of the federal agencies, and the auspicious beginning that give promise of effective planning and management of the Government's expanding scientific and technological activities.

Bethe Testifies on New Data, and Their Relationship to Geneva Talks

Speaking before the Joint Atomic Energy Committee's subgroup on disarmament, Hans Bethe, professor of physics at Cornell University and member of the President's Science Advisory Committee, gave his views last month on certain scientific findings that have bearing on the armament control talks now underway in Geneva, Switzerland. Bethe said that he would like to see the manned surface seismographic stations that are now being considered supported by many robot stations both on the surface and in deep wells around the earth. Bethe's testimony, which was well received by the subcommittee, covered many aspects of the related problems of nuclear weapon testing and detection.

The testimony was presented 2 February and was released later in the month after classified material had been deleted. Two passages from the transcripts of the hearings are published here.

Effect of Data on Geneva Conclusions

Senator Hubert Humphrey (D-Minn.), chairman of the subcommittee: "What Dr. Bethe is attempting to help us with today, is the effect of the new data upon the conclusions drawn by the Geneva Conference of Experts."

Bethe: "That is what I hope to say."

Humphrey: "As you know some people said that the new data necessitated a complete reevaluation of what had taken place at Geneva last summer. They have said that the conclusions last summer have been made invalid because of the new explosions, since the conclusions last summer at Geneva were based pretty much on the Rainier test, plus the theoretical knowledge we had, plus the knowledge about earthquakes and nonnuclear explosions."

Bethe: "Yes."

Humphrey: "But with these four nuclear explosions last October, new data were obtained, and some people have said that the new data literally washed out all that had been accepted as true before. What Dr. Bethe is saying is that the new data didn't affect the first zone [0 to 600 miles] or the second zone [1400 miles and further], but it did show up a few tracings in the shadow zone [600 to 1400 miles]. Is that right?"

Bethe: "That is correct, except that I said that the magnitude of the signal in the first and second zone was less than . . ."

Humphrey: "Than they had anticipated."

Bethe: "Than they had anticipated."

Humphrey: "In other words, the larger explosions theoretically should have yielded a larger magnitude in the first zone and the second zone."

Bethe: "That is correct."

Humphrey: "But they did not. In other words, the practical experience did not fully substantiate the theoretical conclusions."

Bethe: "That is correct."

Humphrey: "However, the practical experience did not destroy the theoretical evaluations."

Bethe: "That is also correct."

Humphrey: "It only turned out to be a little less."

Bethe: "That is correct."

Humphrey: "In other words, the assumptions were greater than the fact."

Bethe: "That is correct."

Result of October Tests

Bethe: "This is what I want to testify to, just this problem. The main result of the October tests in Nevada was not what I said before, but the main result was that the first motion of the earth as recorded by the seismograph is reduced to about 40 percent of what we previously expected. Now the first motion is important because this is the way we tell

explosions from earthquakes. In explosions, as I told in my previous testimony to you, the first motion is always outward. You push the earth away by the explosion, and you observe this outward motion at all seismic stations wherever you are. In an earthquake, on the other hand, you get an outward motion in some directions and an inward motion in other directions, and therefore, if you can observe the seismic signal at many stations, then you can tell an earthquake from an explosion by observing carefully the first motion. If you find that at all stations the first motion is positive, as we say, outward, upward, then you have an explosion. If you observe that it is positive at some stations and negative at other stations, then you have almost surely an earthquake.

"Now the Geneva Conference of Experts did not write this conclusion down in detail, but generally agreed in the discussions that in order to identify an earthquake one should observe two negative motions: one should have at two seismic stations a clear negative signal, downward signal, where the earth first moves down and then comes back up again. So it is the first motion which permits you to tell an explosion from an earthquake.

"Now why is that important? It is important because there are hundreds of earthquakes each year which give as big a signal as the explosions that we are concerned about, and therefore we must be able to distinguish the earthquakes from the explosions, and the best way we have found so far is this first motion. This is not the only way, but it is the best way, the most established way."

Education Act Hearings Stir Altercation on Security Clauses

In hearings before the Committee on Education and Labor of the House of Representatives a wide range of testimony has been presented recently on the progress of the National Defense Education Act of 1958. Officials from the U.S. Office of Education spoke on the implementation of the various titles of the act and discussed some of the problems that have arisen. One subject, the controversial loyalty oath and disclaimer clauses, caused an exchange that brought out the positions of a number of committee members.

Many members of the academic community are opposed to these clauses on the grounds that the first is unnecessary and that the second implies that the student is a "particularly suspect part of the population" who must pass a special test not required of other citizens. The exchange on the two security sections of the act, taken from a stenographic transcript, follows.

Frank Thompson (D-N.J.): "I think before we leave the loan fund I would like to ask Mr. Derthick whether he shares the feeling expressed by Secretary Flemming on about December 15, concerning the loyalty oath provision of this act."

Lawrence Derthick, U.S. Commissioner of Education: "I do."

Thompson: "In other words, you feel they are not necessary?"

Derthick: "I do."

Thompson: "I am very glad to hear that. Mr. Frelinghuysen (R-N.J.), has legislation which would eliminate it. I have it, and others do.

"I note with some interest I have communications from a great many institutions, the president of Yale University wrote a beautiful letter to the Secretary in this connection, which I think should be made a part of the record, Mr. Chairman, and I would like to do that.

"Princeton, Harvard, Yale, Bryn Mawr, three colleges in Maine, and numerous others, have expressed themselves as not being interested in participating in the loan features of the act if the loyalty oath remains."

Graham Barden (D-N.C.), chairman of the full committee: "Mr. Chairman?"

Cleveland Bailey (D-W.Va.), chairman of the subcommittee on general education and the presiding officer: "Mr. Barden."

Barden: "Mr. Chairman, I would not like for that exchange of remarks to go by as though it had the unanimous approval of this committee, because as a member of the committee I shall resist with everything that is within me the removal of that provision.

"Now, I have heard enough of this, every time we pass a law there is somebody who wants to come in and grab the money. They are interested in the money, then they want to raise a great howl over taking an oath of allegiance to America.

"I have been signing and swearing allegiance to America ever since I was a Boy Scout; did so when I entered the service in World War I, and have done so thousands of times since, including the oath that I did not belong to any organization that advocated or taught the overthrow of my government.

"When I became a member of Congress I took an oath. Every clerk or employee connected with this Congress, everyone who works for this government, takes that kind of oath, now up comes a bunch of college professors thinking it is so horrible and terrible to have to say they will not belong or do not belong to an organization that teaches the overthrow of this government.

"Here we are pouring out billions of dollars to teachers and professors to teach people. Are they going to instruct kids that they do have a right to belong to organizations that teach the overthrow of this government?

"I shall resist the removal of these obligations with everything there is in me. I do not think that is going to make any loyal citizen out of anybody, but the very fact that somebody raises the question and resists making a full declaration of loyalty raises some question in my mind. Now, I could not sit here and let that go."

Thompson: "I can understand the chairman's sentiments. I might point out that as well as is known, I doubt that a practicing communist would have any hesitation on swearing on any number of Bibles that he was not a communist."

Braden: "It will not hurt him to tell one more lie which he will gladly do."

Bailey: "Gentlemen, we will thresh this out in executive session when we are ready to vote on this bill."

John LaFore (R-Pa.): "For the record, I would like to associate myself with the chairman and his remarks."

Dominick Daniels (D-N.J.): "I do likewise."

Robert Griffin (R-Mich.): "Mr. Chairman, before we leave this section, because it deals with the administration of the acts, I would like to ask the commissioner, how are you administering this particular provision? It says that an affidavit shall be filed with the commissioner. Has a form been drawn up and is this thing in operation now?"

Derthick: "Let me say that our position does not object to the first part of this requirement. The oath of allegiance we don't object to that at all. Dr. Babbidge, would you report in response to Mr. Griffin's question?"

Homer Babbidge, an assistant to Derthick in the Office of Education: "Forms have been developed in connection with each program under which students received assistance. They will be required to fill out the form."

Griffin: "May I suggest that it be inserted in the record at this point."

Babbidge: "We will be very happy to do so."

Roy Wier (D-Minn.): "Mr. Chairman, I see a difference here of a point of view. I have no objection at all to the allegiance to the United States, but the communists, they are something else again. I think everybody here ought to take an allegiance, but the allegiance and the communist oath are two different things."

Barden: "As long as I am willing to do what I have done, and that is bare my chest to the bullets of enemy nations, I am willing to take any oath and preserve it and keep a screwball from getting into a position of spreading some kind of propaganda or something that will harm my government. I feel that very strongly.

"I must say this: I think Mr. Flemming should entertain himself in some other manner than attacking these requirements which were approved and passed by the Congress of the United States, and signed by the President.

"We are representatives of the people and we, likewise, are servants like the rest. So I am not so fond of Mr. Flemming's attack. If he has a suggestion to make about it, the committee is the proper place to do it and not shower that kind of stuff on members of Congress who are doing the best they can to safeguard and protect this country from every type of enemy or termite that might relish an opportunity to dig from within."

Australian Atomic Institute

The inaugural meeting of the Australian Institute of Nuclear Science and Engineering was held on 4 December at the headquarters of the Australian Atomic Energy Commission, Coogee, New South Wales.

At the meeting, the institute formally came into being when its constitution was unanimously adopted by its founding members, comprising every Australian university and the commission. Through the institute, the commission will allow universities to use nuclear research reactor HIFAR and other equipment and facilities at the Lucas Heights Research Establishment which is near Sydney. The institute will be managed by a council of commission and university representatives and a small permanent secretariat. The council, through the secretariat and in association with the commission, will organize research projects and training courses for university staff members and students at Lucas Heights.

The Commonwealth Government has provided £60,000 for a headquarters building at Lucas Heights. This will include a lecture hall, study rooms, and offices and will be ready for occupation by mid-1959.

The objectives of the institute, as set out in the rules adopted by the inaugural meeting, include the carrying out of research and investigations in connection with matters associated with uranium or atomic energy; arrangements for the training of scientific research workers and the establishment of scientific research studentships and fellowships in matters associated with uranium or atomic energy; the collection and distribution of information relating to uranium or to atomic energy; the publishing of scientific and technical reports, periodicals, and papers in connection with the activities of the institute and other similar activities.

The meeting elected as first president of the institute, D. O. Jordan, professor of physical and inorganic chemistry at the University of Adelaide. Vice-presidents will be representatives of the universities of Melbourne and New South Wales.

News Briefs

The Atomic Energy Commission has established an awards program for outstanding top-management contractor employees upon their retirement. Its purpose is to formally recognize noteworthy performance and length of service. The award will be a parchment scroll. It will be given to management employees who have performed outstanding service under an AEC contract for an extended period of time and who retire from the contractor organization while they are still engaged in AEC work.

* * *

The National Broadcasting Company's television program on weather, "The Unchained Goddess," is being repeated on 22 March. This hour-long Bell System program, which was directed by Frank Capra, explains weather fundamentals with the help of animated characters and charts. Meteorologists Bernhard Haurwitz and Morris Neiburger were technical advisers.

* * *

The Columbia University School of Engineering's new program of college-level science courses for gifted high-school students, inaugurated last fall, has met with such success that plans are under way to make it permanent if sufficient financial support is forthcoming. An expanded class, with possibly a dozen high-school science teachers as observers, is in prospect for the 1959–60 academic year. High schools within commuting distance of New York may nominate students during the spring.

Scientists in the News

JAMES B. CONANT, chemist and president emeritus of Harvard University, has been presented the 1959 Tuition Plan Award for outstanding service to education, in tribute to his 2-year study of American high schools. The award was presented before an assemblage of education leaders at the organization's 19th annual luncheon forum at the Sheraton-East Hotel in New York.

Conant was cited for his "very special service to education" through what has been termed the most extensive examination of the American high school ever made. The findings of his study, financed by grants of $370,000 from the Carnegie Corporation, are detailed in his formal report, *The American High School Today*.

WILLARD F. LIBBY, scientist member of the U.S. Atomic Energy Commission who recently announced that he will resign in June, received Dickinson College's annual $1000 Priestley Memorial Award on 19 March. Libby, a nuclear chemist, was the first to find carbon-14 atoms in nature. He is the founder of radiocarbon dating.

GEORGE E. UHLENBECK, professor of theoretical physics at the University of Michigan and codiscoverer with Samuel E. Goudsmit of Brookhaven National Laboratory of electron spin, has been elected president of the American Physical Society. He succeeds JESSE W. BEAMS, professor of physics at the University of Virginia.

R. WINSTON EVANS, pathologist in the department of clinical pathology at the University of Liverpool, England, has been named visiting professor of pathology at the University of Chicago. He is the author of *Histological Appearances of Tumours*.

NORMAN KRETCHMER, associate professor of pediatrics at Cornell University Medical School, has been appointed head of Stanford University's pediatrics department, effective 1 July. He will succeed ROBERT H. ALWAY, dean of Stanford University Medical School. RUTH T. GROSS, associate professor, has been acting head of the pediatrics department for the past 2 years.

A competition designed to encourage improvement of apparatus for physics teaching was held at the recent annual meeting of the American Association of Physics Teachers in New York, under the sponsorship of the association's committee on apparatus and with the support of the W. M. Welch Scientific Co.

The first prize of $500 in the lecture-demonstration category was won by HAROLD M. WAAGE, of the physics department at Princeton University, for a beat analysis using an optical pendulum.

The first prize of $500 in the laboratory category was won by WILLIAM M. WHITNEY and ROBERT G. MARCLEY, both of the physics department of Massachusetts Institute of Technology; for air-suspended collision disks for studying conservation of momentum.

CLARE P. STANFORD, formerly of the Westinghouse Electric Company's Atomic Power Division, has been appointed chief of the engineering department in the nuclear division of the Martin Company, Baltimore, Md. He succeeds J. A. HUNTER, who has been assigned to the office of the vice-president for engineering.

GORDON E. DUNN, Weather Bureau meteorologist in charge of the Miami Hurricane Forecast Center, has received a gold medal citation for his contributions to the field of hurricane warnings. The citation was presented at the 11th annual Awards Program of the U.S. Department of Commerce, Washington, D.C.

DORSEY E. HOLTKAMP, senior research scientist with Smith, Kline and French Laboratories, Philadelphia, Pa., has been appointed head of the department of endocrinology of the Wm. S. Merrell Company, Cincinnati, Ohio.

JOHN M. BLOCHER, Jr., for 12 years a member of the research staff at Battelle Memorial Institute, Columbus, Ohio, has been appointed chief of the institute's division of inorganic chemistry and chemical engineering.

JOHN R. BEEM, assistant professor of medicine and director of the hypertension renal section at Hahnemann Medical College and Hospital, Philadelphia, Pa., has been appointed director of clinical research at the Warner-Lambert Research Institute, Morris Plains, N.J.

JOSEPH E. RALL, chief of the clinical endocrinology branch of the National Institute of Arthritis and Metabolic Diseases, Bethesda, Md., has received the Arthur S. Flemming award. He was cited for research which has provided new information on the chemistry of the hormones secreted by the thyroid gland and on the effects of these hormones on tissues.

MERVIN J. KELLY and WALTER H. FREYGANG were presented the 1959 Stevens Honor Awards at the annual dinner of the alumni association of the Stevens Institute of Technology, which took place on 26 February in New York. Kelly is chairman of the board of Bell Telephone Laboratories, and Freygang is president and director of the Kidde Manufacturing Company.

HARRY HARLOW of the University of Wisconsin will discuss "The Intellectual Development of the Infant Monkey" as a Sigma Xi national lecturer at a number of colleges and universities during March and April.

RUTH FOX, psychoanalyst, has been named medical director of the National Council on Alcoholism, 2 E. 103rd St., New York. Dr. Fox performed pioneering research on the use of Antabuse.

ALFRED S. EVANS, director of the preventive medicine section of student health and associate professor of medical microbiology at the University of Wisconsin Medical Center, has been appointed chairman of the newly established department of preventive medicine and director of the State Laboratory of Hygiene. He succeeds WILLIAM D. STOVALL as director of the hygiene laboratory. Stovall, who has headed the unit for more than 30 years, will serve as acting director until 1 September to allow Evans to study epidemiology and public health at the University of Michigan School of Public Health.

JOSEF BROZEK, associate professor in the Physiological Hygiene Laboratory at the University of Minnesota, has been named head of the department of psychology at Lehigh University. He succeeds NATHAN B. GROSS, associate professor of psychology, who has been acting head of the department since 1957.

Also at Lehigh, H. RICHARD GAULT, professor of geology, has been named head of the department, effective 1 July. He will succeed BRADFORD WILLARD, who has been department head since 1939.

WILLIAM KAUFMAN of Bridgeport, Conn., American editor-in-chief of the *International Archives of Allergy and Applied Immunology,* has been elected a fellow of the Royal Society of Medicine (England).

PAUL C. BEAVER, professor of parasitology at Tulane University Medical School and a member of the faculty since 1945, has been named to Tulane's William Vincent professorship in tropical diseases and hygiene. He succeeds the retiring ERNEST C. FAUST, who will continue as field coordinator of the Tulane consultant program with the seven medical schools in Colombia, South America.

AKSEL A. BOTHNER-BY has been appointed assistant director of research of Mellon Institute, Pittsburgh, Pa. In his new position he will devote himself principally to the institute's fundamental research program, with primary responsibility for organic chemistry. He will continue to participate in research in theoretical organic chemistry and nuclear magnetic resonance. Bothner-By joined the Mellon research staff last year.

Also at Mellon Institute, WILLIAM C. HUNT has been appointed to the newly created post, head of scientific relations. He has been administrative fellow of the H. H. Robertson Company's Protected Metals Fellowship since 1956. In his new capacity he will provide administrative assistance to the institute's research directors by coordinating relations with sponsors of the fundamental research program.

Recent Deaths

WILLIAM M. COOPER, New York; 64; specialist in vascular surgery and circulatory diseases; former adjunct professor of surgery at Polyclinic Hospital; 16 Feb.

FREDERICK I. DESSAU, Grand View, N.Y.; 49; head pathologist at Lederle Laboratories; educated in Germany; came to the United States in 1938, where he did research work at Yale and Harvard medical schools; joined Lederle in 1943; 23 Feb.

THOMAS L. ECKERSLEY, London, England; 72; research scientist with the Marconi Company from 1919 until his retirement in 1946; worked on the resistance of transmitting aerials and later directed a research team that carried out many pioneering investigations of the ionosphere; 15 Feb.

LUIGI EMANUELI, Milan, Italy; 75; vice chairman of Pirelli, Italy's leading manufacturer of tires and submarine cables; joined Pirelli in 1907 as research engineer in the cable department; designed the first length of oil-filled cables for the insulation of high-voltage electric current and made many improvements in submarine telephone cables; 17 Feb.

ANDREW J. MOYER, St. Petersburg, Fla.; 59; microbiologist with the U.S. Department of Agriculture since 1929; devised methods for producing an increase in the yields of penicillin; 18 Feb.

Sir OWEN W. RICHARDSON, London, England; 79; director of research in physics at King's College, London University, 1924–44; winner of the Nobel Prize for physics in 1928; 15 Feb.

PIERRE RYCKMANS, Brussels, Belgium; member of the Belgian Atomic Energy Commission and a pioneer in nuclear energy development; played an important role in the establishment of the International Atomic Energy Agency; 20 Feb.

MATTHEW TAUBENHAUS, Chicago, Ill.; 55; vice chairman of the department of medicine at Michael Reese Hospital, Chicago; before joining the hospital in 1939, practiced internal medicine in Vienna, Austria; 16 Jan.

SEYMOUR D. VESTERMARK, Washington, D.C.; 56; chief of the training branch of the National Institute of Mental Health from 1948 to 1958; participated in a pioneer field investigation of the epidemiology of mental disorders in Lexington, Ky.; 23 Feb.

ERNST K. WINTER, Tappan, N.Y.; 63; professor of sociology at the University of Vienna since 1955; professor of sociology and social philosophy of the Graduate School at the New School for Social Research, 1938–55; vice mayor of Vienna from 1934 until 1938, when he left Austria and came to the United States; 4 Feb.

Book Reviews

Peace without Victory. Woodrow Wilson and the British liberals. Laurence W. Martin. Yale University Press, New Haven, Conn., 1958. xi + 230 pp. $4.50.

Although much has been written about the sources of Woodrow Wilson's views on foreign affairs, one important influence which has not previously been described in detail was that exerted by the radical wing of British liberalism. In a scholarly, readable book, Laurence W. Martin, who teaches political science at Massachusetts Institute of Technology, has traced the interplay of ideas between the American President and the British radicals, a relationship which began early in 1915 during Colonel House's mission to Europe and which continued throughout the war years. Martin has prefaced his account with a brief but informative discussion of the liberal inheritance that was shared by Wilson and the radicals.

The outbreak of hostilities in 1914 profoundly shocked the Liberal party. The majority of its supporters quickly rallied behind the Government and accepted the position of Asquith and Grey that Britain had no choice but to join her Continental allies in opposing the Central Powers. However, a highly articulate minority of politicians, journalists, and publicists—know as the radicals—were critical of the decision to enter the war. The radicals blamed the "system" of diplomacy and power politics more than the aggressive designs of any one country, thus expressing a traditional liberal view of foreign affairs and one that had been developed in the writing of such students of international relations as J. A. Hobhouse, Norman Angell, and E. D. Morel. Through the press and in parliamentary speeches the radicals warned their countrymen that a military victory alone would not ensure a lasting peace; a new approach to world problems was required. In President Wilson they saw a powerful ally. As the leader of the strongest neutral nation, he could exert influence on the belligerent governments and induce them to think in terms of "peace without victory."

These were views to which Wilson was receptive. The President began to draw ideas from the radicals, and they in turn gave support to his efforts at mediation, elicitation of war aims, and formulation of conditions for peace. Some of Wilson's speeches after the American declaration of war troubled the radicals, but they found reassurance in his Fourteen Points. He carried to the peace table their hopes for reasonable terms and a new international order.

The realization of many of the aspirations of Wilson and the British radicals was frustrated, as the author indicates, by the difficulty of applying "liberal precepts to the real world of fear, ambition, and unaccommodating geography," and by the popular passions aroused during a long and bloody conflict. Nevertheless, their approach to international affairs has remained influential on both sides of the Atlantic.

HIRAM STOUT
Washington, D.C.

The Geology of Uranium. Supplement No. 6 of the *Soviet Journal of Atomic Energy*, Atomic Press, Moscow, 1957; translated from the Russian. Consultants Bureau, New York, 1958. vi + 128 pp. Illus. $6.

The title of this translation is a misleading abbreviation of the Russian title, *Problems in the Geology of Uranium*. The book makes no pretense of being what the English title implies—a comprehensive treatise on uranium geology—but is simply a modest collection of a dozen papers by various authors on a few topics related to uranium.

The first three papers are detailed descriptions of specific occurrences of uranium ore and are marred only by the fact that they contain no geologic maps and no indication as to where the deposits are located. The first two concern bedded deposits in metamorphosed clastic sediments of Paleozoic age. As is so often true of such deposits, the relations of ore to sedimentary structures, tectonic structures, and intrusive contacts permit a variety of interpretations; the authors favor concentration of uranium by metamorphism of original uranium-rich sediments but recognize that the evidence is not conclusive. The third paper describes a uranium occurrence in folded Jurassic sandstones and coal beds, where field relations suggest deposition of uranium from ground water moving through permeable beds, the uranium being derived by leaching of adjacent granites and being deposited by adsorption and reduction by the organic compounds in coal.

The next four papers are technical descriptions of new uranium minerals—the silicates nenadkevite and ursilite and the phosphates uramphite and natroautunite. The eighth paper describes the artificial production of uraninite by heating a slice of carbonaceous shale in a dilute uranium solution to 300°C, and the ninth paper is a survey of experiments on the thermal behavior of minerals of sexivalent uranium. The next two papers are concerned with a method of determining uranium in ores by measuring beta and gamma radiation. The final paper is a résumé for Russian readers of the methods of aerial radiometric prospecting used in the United States, Canada, and Australia.

The articles provide a good sample of the kind of geological and mineralogical work being done on uranium deposits in Russia. The similarity to current work in this country is most striking—the same questions are being asked, the same hypotheses are being weighed, and the same combination of field and laboratory techniques is being used. In comparison with recent American papers of the same sort, two differences are notable: The Russian papers in general are more loosely organized and more repetitive, suggesting that the authors are under less editorial pressure to express themselves as concisely as possible, and the Russian authors make far more use of current American literature than American authors do of Soviet literature.

Consultants Bureau should be commended for a translation that is readable and technically accurate (except for a few minor slips) and for excellent reproductions of photographs and drawings from the original papers.

KONRAD B. KRAUSKOPF
School of Mineral Sciences, Stanford University

Handbuch der Physik. vol. 38, pt. 1, *External Properties of Atomic Nuclei*. S. Flügge, Ed. Springer, Berlin, 1958. vi + 471 pp. Illus. DM. 118.

A sufficient number of volumes of the new edition of the *Handbuch der Physik* have appeared to provide a clearer picture of the magnitude of the task. The tremendous expansion in physics research in the past 25 years has posed serious problems for the systematizers of knowledge. Should articles be devoted to currently popular models of nuclei which may change drastically in a few years? How detailed should the papers be?

Should one devote space to compilations of data?

Since the last edition of the *Handbuch,* physics writing has expanded so that we are bombarded continually with reviews, surveys, and tabulations of data. Most of these appear as journal articles—a form befitting their ephemeral status. The lifetime of a compilation is now not 25 years but at most 3 or 4 years. Of more lasting importance are the excellent books we now have on many special topics.

The papers which made the earlier *Handbuch* a classic were those which presented thorough discussions of principles and ideas, on dynamics, thermodynamics, and electromagnetic theory. In particular, the papers of Pauli and Bethe served (and still serve) as the prime texts for quantum mechanics. The new edition has preserved these beautiful articles and added some new ones of comparable caliber, but the chopping up of many subjects has made the *Handbuch* resemble, in places, a handbook of formulas and tables, with cross references from one incomplete presentation to another.

I can offer no good solution to the encyclopedists' dilemma.

The principal article in the present volume is by G. Laukien, on high-frequency nuclear resonance spectroscopy. It gives a thorough, self-contained presentation of a whole new field which has developed since 1945. The discussion of solutions of the equations of motion is excellent. Circuits and experimental techniques are compared and criticized. Especially good is the discussion of precision measurements of the proton moment. The article concludes with a tabulation of nuclear moments.

For lack of space, I shall only enumerate the other, shorter articles included in the present volume: "Atomic masses of nuclides," by A. H. Wapstra; "Determination of atomic masses by microwave methods," by S. Geschwind; "Determination of nuclear spins and magnetic moments," by F. M. Kelly; "Isotope shifts," by L. Wilets; and "Determination of nuclear quadrupole moments," by C. H. Townes.

MORTON HAMERMESH
Argonne National Laboratory

Agricultural Botany. N. T. Gill and K. C. Vear. Duckworth, London, 1958 (order from Macmillan, New York). viii + 636 pp. Illus. $12.

To cover in a not too voluminous textbook such widely ranging subjects as plant breeding, crop improvement, agricultural taxonomy, weed control, and plant diseases, the authors were forced to spread treatment of the subject matter rather thin.

The concise but illuminating chapter on plant genetics and the very informative chapter on crop diseases will be welcome to the general reader. However, where more specific matters, such as the classification and description of farm crops, are involved, the book will appeal to the student of British agriculture, as it deals in a very exhaustive way with crops of economic importance to that country, but it will not be found adequate by students of non-European, especially American, agriculture. To devote only five lines to discussion of the genus *Nicotiana* (page 219) and four lines to the genus *Saccharum* (page 292), and to omit all mention of the genus *Gossypium,* to give but a few examples, diminishes the usefulness to the American reader of an otherwise well-written book.

FRANCIS JOSEPH WEISS
Arlington, Virginia

Robert Boyle and Seventeenth-Century Chemistry. Marie Boas. Cambridge University Press, New York, 1958. viii + 240 pp. $5.50.

Ten years ago, Marie Boas published her doctoral thesis, *Robert Boyle and the Corpuscular Philosophy* (Cornell University, 1949); a revised version appeared in *Osiris* [**10**, 412 (1952)]. With this background, and after additional studies of the Boyle papers in the Royal Society library, Boas now presents a profound yet very readable book on the chemical work of Robert Boyle. Starting with a detailed biography, the author goes on to explain what chemistry was and why Robert Boyle set himself the task of showing "that chemistry was a respectable part of natural philosophy, and that it could contribute to the advancement of natural philosophy as a whole" (page 68). "Alone among natural philosophers professing a particulate theory of matter, Boyle was a chemist using chemical evidence to support his theory" (page 75).

Chapter 3 is a fine exposition of the historical background, with an outstandingly clear account of the Aristotelian theory of forms and qualities. Yet this chapter, like some of the four chapters that follow, is marred by a kind of critical attitude which measures Boyle's achievement against our "better knowledge" of today, and which applies a sort of teleological thinking, as if Boyle were a "predecessor" in a real sense (page 141 and elsewhere). This attitude makes Boas sometimes quite impatient with her hero. Why did he not continue when he was so close to discovering the real nature of the supposed conversion of water into earth upon long boiling in a glass vessel? He knew and described all the principles of the experiments, but he left it to Lavoisier to apply them! Why did he not follow through in his discussion of the elements; why did he remain skeptical instead? Why did he spread his activities so far, when he should have concentrated on what the author believes he should have pursued? Boyle "had not thoroughly learned the fact that it is better to look for limited answers first" (page 107). Such dramatization seems out of place in a historical study. Would it not be better, because more realistic and reasonable, to ask whether men of the 17th century, or at least of Boyle's kind, needed the broad approach to be creative?

In discussing the famous passage from *The Sceptical Chemist* (1661) in which Boyle tells what he means by "Elements," Marie Boas points out that the difference between the concepts of elements then and now must be realized, "and this scholars have not clearly done" (page 96). It may be dramatic but it is not very gracious to make such a condemning general statement. The author makes several statements of this kind; she would have done better to omit them, unless she could go into specific details.

After raising these objections, I am happy to return to the many great merits of this book. It presents the most important of Boyle's thoughts and experiments in historical depth, with many quotations from printed and from unpublished material. Even those who believe they know "their" Boyle will find much enlightenment here, and those who are interested in the evolution of the corpuscular theory, in the relationship between ideas and experiments, or in the intimate picture of a creative mind, whether of the 17th century or any other, will be greatly stimulated by Boas' story, told in the somewhat "rambling and repetitious" (page 212) way of Robert Boyle himself.

EDUARD FARBER
Washington, D.C.

Sewerage and Sewage Treatment. Harold E. Babbitt and E. Robert Baumann. Wiley, New York; Chapman and Hall, London; ed. 8, 1958. viii + 790 pp. Illus. $10.75.

The impact of a new and younger author is evident in this latest edition of a book which has served sanitary engineering well since 1922. A number of changes are evident, in particular the inclusion of more of the modern industrial waste treatment processes and discussion of some of the newer concepts of activated sludge. The presentation of principles of biochemical oxidation and anaerobic fermentation is still somewhat weaker than the student and teacher would like to see.

The first 322 pages, with the exception of a chapter on pumping, deal with the design, construction, maintenance, and operation of sewers. This lengthy discussion of construction methods may make the book more worth while for practicing engineers but adds a great deal of material which may be considered extraneous in an undergraduate course in a modern college of engineering, where greater emphasis is placed upon the scientific principles underlying the practice of engineering. However, the wise teacher will find more than sufficient instructional matter in this book for a good undergraduate course in the collection, treatment, and disposal of sewage and industrial wastes.

ROLF ELIASSEN
Department of Civil and Sanitary Engineering, Massachusetts Institute of Technology

Food Microbiology. William Carroll Frazier. McGraw-Hill, New York, 1958. ix + 472 pp. Illus. $9.

This up-to-date volume is designed, as the author indicates, to be used as a college textbook in the field of food microbiology. For this purpose, the book has merit. It is also a volume that many older workers in the field of food preservation and technology may find valuable as brush-up reading. It is a good digest of microbiology in fields related to the food industries.

Part 1 succinctly describes the microorganisms that are important in food microbiology. The photographs and illustrations dealing with molds, yeasts, and bacteria are of particular interest. In the latter chapters of this section microbiological contamination of food from handling, processing, and natural sources is covered.

Part 2 deals with the preservation of foods. While this text does not go quite far enough into some of the procedures mentioned, it meets the need for which it was designed and covers the field on most types of foods.

Part 3 deals adequately with spoilage of foods. It is readable, yet technical enough to fulfill its purpose. Again, the different foods are treated in separate chapters.

Foods and enzymes produced by microorganisms are described in Part 4 of the text. Culture production and specific food fermentations are also part of this section.

In Part 5 the author rather thoroughly discusses food poisonings and infections. A chapter on the investigation of food-poisoning outbreaks is included.

The sixth section of the book deals briefly with bacteriological aspects of plant sanitation, methods used in microbiological laboratories, and enforcement and control agencies.

The basic principles of food microbiology are adequately digested in this text. It certainly will not replace Tanner's *Microbiology of Foods* as a reference volume, but it should be a welcome modern addition to many classrooms and libraries.

C. B. DENNY
Bacteriology Laboratory, National Canners Association

Fellowships in the Arts and Sciences, 1959–60. Virginia Bosch Potter. Fellowships in the Arts and Sciences, 79 Biochemistry Building, University of Wisconsin, Madison, ed. 2, 1959. viii + 195 pp. $3.75.

This directory, a project of the Association of American Colleges with the cooperation of the Association of Graduate Schools in the Association of American Universities, was made possible through the aid of grants from the following groups: the Danforth Foundation, the Ford Foundation, the National Institutes of Health, the National Science Foundation, and the Rockefeller Foundation.

The directory offers descriptions of fellowships from private foundations, government agencies, professional societies, industry, and other sources outside the universities themselves. Fellowships are listed under the following headings: "Predoctoral"; "Postdoctoral"; "Senior, faculty and special awards"; "Study abroad"; "Summer study"; and "Loans." Subheadings under each of the sections include the following divisions: general, humanities, natural sciences, social sciences, brief listings, and a cross-reference list.

For each major fellowship program listed the following information is given: address of the group administering the awards; purpose; fields included; qualifications of the candidate; period of the award; stipend; other allowances; conditions; type of application; method of review; time schedule; and approximate number of awards.

New Books

Astronomy. A textbook for university and college students. Robert H. Baker. Van Nostrand, Princeton, N.J., ed. 7, 1959. 555 pp. $6.95.

Basic Geology for Science and Engineering. E. C. Dapples. Wiley, New York; Chapman & Hall, London, 1959. 616 pp. $9.50.

Cahiers de synthèse organique. Méthodes et tableaux d'application. vol. 5, *Dégradations.* Léon Velluz, Masson, Paris, 1959. 394 pp.

Dairy Cattle, Judging and Selection. William W. Yapp. Wiley, New York; Chapman & Hall, London, 1959. 334 pp. $5.95.

Dynamics of Flight. Stability and control. Bernard Etkin. Wiley, New York; Chapman & Hall, London, 1959. 533 pp. $15.

The Evolution of Living Things. H. Graham Cannon. Thomas, Springfield, Ill., 1958. 190 pp. $3.50.

Fishes of the Great Lakes Region. Bull. No. 26. Carl L. Hubbs and Karl F. Langler. Cranbrook Inst. of Science, Bloomfield Hills, Mich., rev. ed., 1958. 224 pp. $5.

A Guide to Nuclear Energy. R. F. K. Belchem. Philosophical Library, New York, 1958. 84 pp. $3.75.

Liquid Helium. K. R. Atkins. Cambridge Univ. Press, New York, 1959. 322 pp. $11.

Minnesota's Changing Geography. John R. Borchert. Univ. of Minnesota Press, Minneapolis, 1959. 197 pp. $4.25.

Nomograms for Chemical Engineers. O. P. Kharbanda. Academic Press, New York, 1958. 258 pp. $15.

Nutrition of the Legumes. Proceedings of the University of Nottingham's fifth Easter school in agricultural science, 1958. E. G. Hallsworth, Ed. Academic Press, New York; Butterworths, London, 1958. 369 pp. $10.50.

Optical Properties of Semi-Conductors. T. S. Moss. Academic Press, New York; Butterworths, London, 1959. 289 pp. $9.

Physiological Adaptation. A symposium held during the meeting of the Society of General Physiologists at the Marine Biological Laboratory, Woods Hole, Mass., 5–6 September 1957. C. Ladd Prosser, Ed. American Physiological Soc., Washington, D.C., 1958. 185 pp. $4.

Radioactivity Measuring Instruments. A guide to their construction and use. M. C. Nokes. Philosophical Library, New York, 1958. 83 pp. $4.75.

The Simplicity of Science. Stanley D. Beck. Doubleday, Garden City, N.Y., 1959. 212 pp. $3.75.

Taschenbuch der Botanik. vol. I, *Morphologie, Anatomie, Fortpflanzung, Entwicklungsgeschichte, Physiologie*; 291 pp.; $3.05. vol. 2, *Systematik*; 195 pp.; $3.60. Walter Mevius. Thieme, Stuttgart, Germany, 1958 (order from Intercontinental Medical Book, New York 16).

The Transvaal Ape-Man-Bearing Cave Deposits. Memoir No. 11. C. K. Brain. Transvaal Museum, Pretoria, South Africa, 1958. 131 pp.

Tree Fruit Production. James S. Shoemaker and Benjamin J. E. Teskey. Wiley, New York; Chapman & Hall, London, 1959. 463 pp. $6.95.

Type Specimens of Marine Mollusca Described by P. P. Carpenter from the West Coast (San Diego to British Columbia). Memoir 76. Katherine Van Winkle Palmer. Geological Soc. of America, New York 27, 1958. 384 pp.

Umbelliferae of Japan. Minosuke Hiroe and Lincoln Constance. Univ. of California Press, Berkeley, 1958. 144 pp. $2.75.

Virginity, Pre-Nuptial Rites and Rituals. Ottokar Nemecek. Philosophical Library, New York, 1958. 137 pp. $4.75.

Reports

Incidence of Familial Hyperlipemia

Abstract. Familial hyperlipemia is an inherited disease associated with early onset of coronary atherosclerosis. In a survey of a student population in Sweden, an estimated case incidence of 2 to 3 percent was discovered. This study also demonstrates that there is probably a heterogeneity of causes for the primary elevation of blood triglycerides in man.

Familial hyperlipemia is an inherited disease thought to be due to a single gene difference causing a defect in the lipemia clearing system. The disease was first described by Bürger and Grütz in 1932 (*1*), and since that time over 100 cases have been studied; it is generally agreed that the heterozygous condition manifests itself by a delay in the clearing of ingested fat from the plasma, milky serum with elevation of all lipids but mainly of the neutral fats, the appearance of severe atherosclerosis in early adulthood, and occasionally xanthomatosis. The homozygous condition is characterized by hepatosplenomegaly, abdominal crisis, milky serum, childhood atherosclerosis, and xanthomatosis (*2*).

While it is known that the elevated lipid levels are due to an abnormal prolongation of the clearing of ingested fat from the plasma, there is no general agreement about the exact biochemical lesion responsible for the phenomenon. The three leading explanations are absence or diminution of tissue lipoprotein lipase (clearing factor) (*3*), an abnormality of the chylomicrons (*4*), or an inhibition of the lipoprotein lipase system (*5*).

Although there have been a number of individual case reports, until this time no study of the incidence of this disease in an apparently normal population has appeared. During the routine screening examination of entering students, blood samples were obtained from 998 consecutive students at Uppsala University in Sweden (*6*). The students ranged in age from 18 to 60, 95 percent being 19 to 29, and 80 percent being 19 to 23. There were 496 males and 502 females.

The samples were examined for optical density both visually and by the use of a Beckman DU spectrophotometer at a wavelength of 640 mμ, with the red-sensitive photocell. All those students whose plasma showed a density above the lowest photometric level associated with faint visual turbidity were recalled for fasting specimens. Of the 274 students recalled, 269 returned. Their serum was analyzed for optical density as described above, as well as for "total lipids" by the phenol turbidity method of Kunkel, Ahrens, and Eisenmenger (*7*). The latter method was utilized only as a rough screening test and was not interpreted as an indication of true lipid level.

Thirty-six of these students showed an optical density of over 0.080, a phenol turbidity level equivalent to over 800 mg percent of lipid, or both, or borderline elevations in both these tests. These 36 students were recalled again for a complete medical history, physical examination, urinalysis for sugar and albumin, a fat-tolerance test, and a total determination of serum cholesterol. Five other students were chosen at random, and they, as well as two healthy staff members, were exposed to the same series of examinations. For the fat-tolerance tests a meal of 90 g of fat consisting of normal breakfast foods was given, and blood samples were drawn at the fasting level and at 3 and 9 hours after the meal; there was no food intake between the time of the meal and 9 hours later.

Of the 36 students recalled, 16 demonstrated a marked delay in clearing of neutral fat from the serum, and four showed borderline delay in such clearing. These 20 students ranged in age from 19 to 47, 80 percent being 19 to 27; thus they were somewhat older than the original group. Fifteen of these, including the four borderline cases, were male, perhaps indicating that the disease may be more easily discovered in the male, at least in the younger age group.

Five other students were found to have primary hypercholesterolemia, while three students demonstrated elevated serum optical density both before and 9 hours after the meal, but without delayed return to the fasting levels. Eight of the 36 students were found to be completely normal, showing normal fasting levels at this time. It was strongly suspected that they had eaten before the initial (fasting) samples were obtained.

Some of the students showing hyperlipemia, who had been recalled for fat-tolerance tests because of elevated optical density in their initial samples, showed a serum optical density of below 0.080 in the fasting samples of the fat-tolerance tests despite marked prolongation of clearing time. This indicates that the previously chosen borderline for normal had been too high, and that several cases must have been missed. A statistical analysis leads us to suspect that at least 10 more cases of essential hyperlipemia were missed in the original sample because of fasting optical density values below 0.080, but above the true upper limit of normal.

It would appear, therefore, that the incidence of familial hyperlipemia in an apparently normal northern European population is between 2 and 3 percent, probably closer to 3 percent. In view of the increased predisposition to atherosclerosis in this illness, as partly demonstrated by an increased incidence of atherosclerosis at relatively young age in the families of these students, it is felt that this group makes up a fairly sizable proportion of the increasing number of patients with atherosclerosis. This opinion seems to be confirmed by the findings of delayed lipemia clearing in the plasma of atherosclerotic individuals (*8*).

It is strongly suspected that thrombosis and fibrin deposition may be vital factors in the pathogenesis of atherosclerosis. It is of significance in this connection that increased blood coagulation (*9*) as well as inhibition of fibrinolysis (*10*) have been found in hyperlipemia.

It is of special interest that three individuals were found during this study who maintained an elevated optical density of the serum despite the ability to clear ingested fat normally. A study of the cloudy material in the serum of one of these patients has shown it to be a form of lipid, and it may well represent the abnormal chylemicra held responsible for this disease by some investigators. Although we would hesitate to call

---

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

these three subjects familial hyperlipemics, since they clear ingested fat in a normal period of time, it is fairly certain that they would have been included in such a group on the basis of fasting specimens only. This not only points out the importance of the fat-tolerance test in the diagnosis of familial hyperlipemia but also accentuates the importance of recognizing the possible heterogeneity of biochemical causes for the primary elevation of neutral fat in the blood (*11*).

KURT HIRSCHHORN*
ROCHELLE HIRSCHHORN
Department of Medicine,
New York University, Post-Graduate
Medical School, New York
MARCO FRACCARO
JAN A. BÖÖK
State Institute for Human Genetics,
Uppsala, Sweden

References and Notes

1. M. Bürger and O. Grütz, *Arch. Dermatol. u. Syphilis* 166, 542 (1932).
2. L. E. Holt, Jr., F. X. Aylward, H. A. Timbus, *Acta Paediat.* 22, 425 (1938).
3. R. J. Havel, *Intern. Conf. Biochem. Problems Lipids, 3rd Conf., Brussels* (1956), p. 265.
4. L. A. Carlson and L. B. Wadstrom, *ibid.* p. 123.
5. E. Klein and W. F. Lever, *Proc. Soc. Exptl. Biol. Med.* 95, 565 (1957).
6. This study was aided by a grant from the Population Council, Inc., New York.
7. H. G. Kunkel, E. H. Ahrens, Jr., W. J. Eisenmenger, *Gastroenterology* 11, 499 (1948).
8. G. Angervall and B. Hood, *Acta Med. Scand.* 157, 407 (1957).
9. J. C. F. Poole, *Brit. J. Haematol.* 1, 229 (1955).
10. H. B. W. Greig, *Lancet* 2, 16 (1956).
11. A detailed description of our results is in preparation. We wish to express deep gratitude to Dr. Gunnar Wallenius of the clinical chemistry department of Uppsala University for invaluable advice and for the cholesterol determinations.

* Fellow in human genetics of the Population Council and John G. Bergquist fellow of the Amer.-Scand. Society.

18 November 1958

Predaceous Feeding in Two Common Gooseneck Barnacles

Abstract. *Lepas anatifera* and *Mitella polymerus,* while relatively unselective omnivores, behave at times like predatory macrophagous carnivores. Observations suggest a greater range of food size for gooseneck barnacles than is generally suspected and clearly indicate that large organisms, when available, are effectively captured and handled.

Thoracican barnacles are generally considered to feed on *small* organisms and particles of detritus caught by combing the water with highly setose thoracic appendages. Very few observers have described barnacles feeding on larger forms: Darwin (*1*) notes prehensile behavior of the cirri in capturing crustaceans and other prey; Batham (*2*) notes the curling motions of the cirri in *Mitella* (= *Pollicipes*) *spinosus,* which deposit crustaceans "often of no mean size" in the mouth; Brown (*3*) states that in the laboratory *Lepas* will feed on animals even larger than itself; but Gruvel (*4*) is apparently the only worker who has described the coordinated behavior of the cirri and mouth parts of *Lepas* in seizing and ingesting food of various sizes, and his observations have gone largely unheeded. It is the purpose of this report to present evidence that at least two common gooseneck barnacles not only capture and feed upon large prey but, on occasion, show the feeding habits and food-capturing mechanisms, and have the diets, of macrophagous predators, exhibiting a behavior more reminiscent of the lion than of the anteater.

Initial observations made on *Lepas anatifera* in 1951 at the Hopkins Marine Station of Stanford University by one of us (H.S.) have recently been confirmed and extended by further work on this species (by both of us) and on *Mitella polymerus* (by G.H.). In the laboratory, feeding was observed in both species. A large cluster of *Lepas* attached to driftwood was allowed to feed freely for 2 hours on the brine shrimp *Artemia salina* (5 to 11 mm in length) and on the small tide-pool copepod *Tigriopus californicus* (approximately 1 mm in length). A cluster of *Mitella* freshly removed from intertidal rocks was similarly fed these two animals. The gut contents of the barnacles were then examined. *Lepas,* ranging in size from 11.2/7.0 mm (shell length = ratio of total length of capitulum to gut length) to 7.7/4.8 mm, all ingested both *Artemia* and *Tigriopus;* smaller animals, ranging in size down to 3.6/2.3 mm, took copepods only. The largest individual *Lepas* took 56 *Tigriopus* and two *Artemia.* The second largest (10.8/6.8 mm) took four copepods and four brine shrimp. Individuals of *Mitella* greater in size than 5.8/7.2 mm ingested both *Artemia* and *Tigriopus;* smaller *Mitella,* down to 1.6/2.1 mm, took only copepods. Ingested organisms originally longer than the barnacle digestive tract (Fig. 1) were bitten in pieces, folded, or compacted to fit the gut.

How is the prey of these animals captured and handled? Activity of the cirri and mouth parts of these barnacles is most clearly demonstrated in *Lepas,* though the behavior of *Mitella* is similar. Individuals of *Lepas,* immersed in a suspension of *Artemia* and *Tigriopus,* consistently seized the animals with ravenous grabs, lassoing and caging the prey and holding it in their cirri. The six pairs of thoracic cirri may operate together or move quite independently of one another, a behavior not observed in balanoids but previously seen in *Lepas* (*4*), in *Scapellum* and *Verruca* (*5*), and in *Mitella* (*2*). If a brine shrimp contacts the cirri of *Lepas,* there is a total clutching motion of all the cirri; these then contract, forcing the food toward the mouth parts.

When the animals are feeding on smaller organisms, the functions of the individual cirri can be seen. Here the anterior three thoracic appendages, which are equipped basally with spinous pushing brushes, direct food to the mouth parts, where it is gripped and compacted. At the same time copepods may be trapped by individual rami of the last three cirri, which curl around them and hold them in reserve. We noted that one animal held seven copepods in separate coiled posterior rami while ingesting a brine shrimp. *Mitella* has cirri and mouth parts which are anatomically and functionally similar to those of *Lepas.* The cirri are thicker and shorter and, in general, less active than those of *Lepas,* but when cirri are presented with food, their response is quick. Food may be trapped separately by the last three pairs of rami and passed to the very heavily bristled pushing pads at the bases of the second two pairs of cirri and on the rami of the first cirri, which in turn cram it against the mouth parts for compacting and swallowing.

The differences in feeding behavior between *Lepas* and *Mitella* seem to be in accord with their respective ways of life. *Mitella* characteristically occurs in clusters on a fixed rocky substrate exposed to a great deal of wave action. Individuals are generally oriented in fixed positions to receive the down-wash

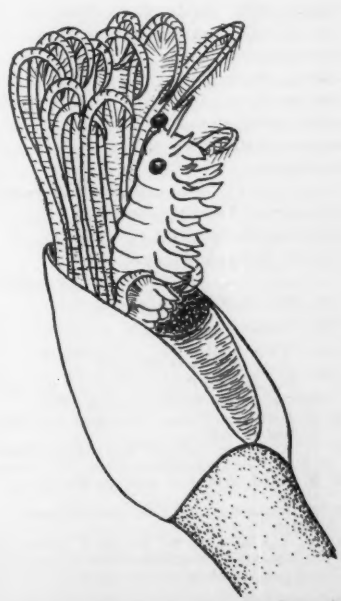


Fig. 1. *Lepas* ingesting *Artemia.*

of waves; cirri are held maximally extended as water, which is often rich in food, sweeps over them. *Lepas,* on the other hand, occurs on freely floating timbers moving *with* the current. The peduncle is highly mobile and swings in every direction; the cirri are more active, though they seldom exhibit the rhythmic beating so characteristic of the balanoids. These motions could be those of foraging, in a situation where the probability of obtaining food by random contact with organisms is greatly reduced (even though at sea certain forms tend to congregate below floating objects).

What is the natural diet of these organisms? Examination of the gut contents from monthly collections of *Mitella* taken over a period of a year showed that copepods, algae, and unidentified particulate matter are nearly always present; cirriped molts, amphipods, cypris larvae, small clams, and hydroids occur frequently; polychaetes and barnacle nauplii are taken occasionally. Batham's list for *Mitella spinosus* is comparable. Polychaetes and plant fragments over one-half the gut length were found coiled inside.

The guts of a number of field specimens of *Lepas* were also inspected, disclosing polychaetes, amphipods, (gammarids, hyperiids, and caprellids), caridean shrimps, gastropods, clams, pycnogonids, algae, and detritus. Some of these items were doubtless captured while the timber bearing the barnacles was washed about in the intertidal zone. The largest crustaceans measured nearly one-half the length of the barnacle gut holding them.

Despite the effective predaceous behavior often exhibited by both *Lepas* and *Mitella,* these forms, as feeders, are opportunistic rather than selective; *Lepas,* attached to timbers stranded on the beach, will fill their guts with sand, while small chunks of granite and calcareous shell have been noted in the gut of *Mitella* (*6*).

GALEN KENT HOWARD
Division of Natural Sciences,
Hopkins Marine Station,
Pacific Grove, California
HENRY C. SCOTT
San Francisco State College,
San Francisco, California

References and Notes

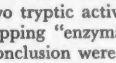
1. C. Darwin, *A Monograph on the Sub-class Cirripedia* (Ray Society, London, 1851).
2. E. J. Batham, *Trans. Proc. Roy. Soc. New Zealand* 74 (1945).
3. F. A. Brown, *Selected Invertebrate Types* (Wiley, New York, 1950).
4. A. Gruvel, *Arch. zool. expil. et gén.* 1, ser. 3 (1893).
5. C. Nilsson-Cantell, *Zool. Bidr. Uppsala* 7 (1921).
6. We wish to thank Dr. Donald P. Abbott of Hopkins Marine Station for his encouragement and generous advice on this project.

9 October 1958

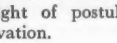
Structural Correlation between Esterase and Protease Activities of Trypsin

Abstract. It is tentatively concluded from ultraviolet and x-ray studies that the two tryptic activities are mediated by overlapping "enzymatic sites." Crucial to this conclusion were studies of the factors which can modify the measured inactivation rates. The data are interpreted in the light of postulated mechanisms of inactivation.

Some enzymes are presumed to have more than one catalytic activity since they act upon substrates that are quite different. Whether these activities are mediated by a single site or a number of separated sites on the enzyme surface is a problem of current biochemical interest and importance. Previous workers concluded that the esterase and protease activities of trypsin (that is, the ability to hydrolyze, respectively, the



structure of esters and the



structure of polypeptides and proteins) must be located at a single site. The evidence is twofold (*1*): (i) Inhibitors of fairly large molecular weight produce equivalent decreases in the two activities, and (ii) trypsin hydrolyzes either type of substrate at a decreased rate in the presence of the other type. However, this evidence does not preclude the existence of closely adjacent or overlapping sites.

The radiation studies reported here were designed to examine this question without use of large-sized inhibitors. Presumably, x-ray inactivation is initiated by radiation-produced radicals of low molecular weight (*2*). Inactivation by ultraviolet irradiation (2537 A) is probably localized within a small region of trypsin, since only one molecule is inactivated per approximately 60 quanta absorbed (each of 4.9 ev). In both studies, the two activities should be inactivated at identical rates if only a single site is involved but probably, although not necessarily, at different rates if adjacent or overlapping sites exist.

The same two activities are inactivated unequally when chymotrypsin is x-irradiated in dilute solution (*3*) or oxidized with sodium periodate (*4*). This has been attributed to concentric sites having different areas or charge configurations (*3*).

While such conclusions are possibly correct, they now appear to require additional justification, since we have found that measured inactivation rates are affected by the treatment afforded irradiated molecules prior to and during assay. Specifically, our experiments are consistent with these postulates: (i) At least three classes of trypsin molecules are present in solution after irradiation—active, damaged, and inactive. (ii) Damaged molecules have an average of one to three more intact H-bonds than do inactive ones and therefore can be converted to the inactive class either by urea ($> 5.5M$) or by thermal treatment prior to the addition of a substrate. (iii) Damaged molecules have normal activity either when only substrate is added or after urea is added if they have been previously exposed to substrate at a *p*H consistent with activity. (iv) This prior exposure to substrate "reactivates" damaged molecules to active ones.

I obtained results similar to those of Aronson, Mee, and Smith (*3*) when 0.4 to 5.0μM solutions of trypsin (twice recrystallized, from Worthington Biochemical Co.) in 0.001M Na_2HPO_4 were irradiated at 0°C with 250 kv (peak) x-rays. Protease activity was determined by hydrolysis of hemoglobin (*5*) (Hb); esterase activity, by hydrolysis of benzoyl-arginine ethyl ester (*6*) (BAEE). The decrease (inactivation) of both activities with increasing dose fitted (± 10 percent) the kinetics of a first-order reaction. The two inactivation rates depend upon the initial trypsin concentration and are quite different. That measured by Hb assay (which employs 5.5M urea) was about 1.5 times that measured by BAEE assay (no urea) when both were extrapolated to infinite solute concentration (*2*). If a one-to-one correspondence between reaction probability and fraction of surface area is assumed, the number of amino acids in the proteolytic site which are reactive to radiation-produced radicals is estimated to be between two and four (*2*).

Only slightly different results were obtained when ultraviolet irradiation instead of x-ray was carried out at 0°C (see plots for H and B, 0° in Fig. 1): the inactivation rates were essentially independent of trypsin concentration between 0.4 and 5.0μM and in a ratio of about 3:1 or 4:1 rather than 1.5:1. The four postulates depend critically upon the following preliminary results with ultraviolet irradiation (see Fig. 1).

1) The rate of inactivation measured by Hb assay appears to be independent of the temperature during irradiation, from 0° to 60°C [see (H, 0–60°)].

2) When samples irradiated at 0° are heated at 60° for 30 minutes (B, 0°:P60°, 30 m) or 100 minutes (B, 0°:P60°, 100 m) immediately after irradiation, and thus prior to assay, the "BAEE-measured rate" approaches the standard "Hb-measured rate."

3) The rate of inactivation measured

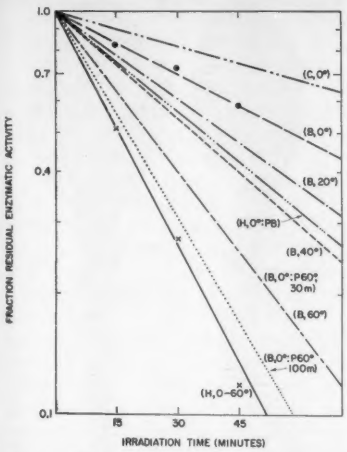


Fig. 1. Effect of temperature, urea, and substrate on the measured level of ultraviolet inactivation of trypsin. The labeling on the curves is explained in the text. Data are shown for only two curves for clarity of presentation; other data showed comparable variances.

by BAEE assay has a ΔH^* of 2500 ± 500 cal/mole from zero (B, 0°) to 60° (B, 60°), approaching the "Hb-measured rate" at 60°C.

4) Without exposure to urea or thermal treatment, an amount of BAEE, which would normally be completely hydrolyzed in 5 minutes, is added in buffer (*p*H 8) 10 to 30 minutes prior to assay; the inactivation rates measured by a subsequent Hb assay are more characteristic of "BAEE-measured rates" than of Hb rates (H, 0°:PB).

The results suggest that radiation causes previously inaccessible H-bonds—necessary for activity—to become available for urea attack or else unstable to the molecular swelling it produces. Thus it appears that the effects of urea or heat, or both, are additive with those of irradiation. This result was predicted previously on the basis of my hypothesis (*7, 8*) that inactivation by physical means proceeds by the sequential rupture of the disulfide and hydrogen bonds making up a "weak-link" structure which is instrumental in "latching" the enzyme together.

The calculated efficiency of 2537-A light in promoting protein inactivation through the rupture of disulfide bonds (*9*) indicates that the data presented here are probably in accord with this hypothesis. Also consistent are the observations of McDonald (*10*) and Monier (*11*) that trypsin molecules having different sensitivities to thermal aging and urea denaturation are produced by x-irradiation of dilute solutions. However, Liener (*12*) recently reported that irreversible trypsin inactivation results from the rupture of only one disulfide bond, rather than my predicted two. This expected correlation between inactivation and increase in —SH titer is now being investigated.

The "reactivation" proposed in the fourth postulate had also been previously anticipated (*8*). However, although my evidence indicates that damaged molecules are reactivated through interaction with BAEE, it is difficult to exclude the possibility that a significant portion of the reversal is produced by the change in *p*H from 4.5 to 8. Probably the reactivation contributions of substrate and *p*H can be best differentiated with a nonproteolytic enzyme, since the possibility of tryptic autodigestion interferes with the interpretation of some of the critical control experiments.

The reversal by BAEE of inactivation which would have been measured by Hb assay indicates that portions of the two activities are probably inactivated by a common mechanism (*13*) (weak link ?). In addition, protease assays employing casein (C, 0°) without urea suggest that the *reactivation capability* differs among substrates. For example, in one experiment the rate of inactivation measured by casein assay (no urea) had a $\Delta H^* = 4750 \pm 500$ cal/mole from 0° to 60°C, as compared with 2500 ± 500 for the BAEE assay.

These and the results cited in paragraphs 2) and 3) above, plus the evidence reviewed in the first paragraph, lead to a tentative conclusion of overlapping sites—where the hydrolytic apparatus would be common but the elements which could form specific attachment would vary with the substrate. Unfortunately, these preliminary results are as yet insufficient for *unequivocal* specification of the architecture of the sites. However, they provide strong evidence concerning some of the steps whereby inactivation proceeds and, therefore, warrant reporting at this time. It is hoped that extension of these studies will permit a specification of the secondary and tertiary structure critical for enzymatic activity as well as define the structural correlation between the two activities.

LEROY AUGENSTINE*
Biology Department, Brookhaven National Laboratory, Upton, New York

References and Notes

1. P. Desnuelle, *Ann. Rev. Biochem.* 23, 55 (1954); G. Schwert, *ibid.* 24, 83 (1955); N. Green and H. Neurath, *The Proteins* (Academic Press, New York, 1954), vol. IIB, pp. 1057–1198.
2. L. Augenstine, *Radiation Research*, in press.
3. D. Aronson, L. Mee, C. Smith, in *Progress in Radiobiology*, J. Mitchell, B. Holmes, C. Smith, Eds. (Oliver and Boyd, Edinburgh, 1955), pp. 61–69.
4. E. Jansen, A. Curl, A. Balls, *J. Biol. Chem.* 189, 671 (1951).
5. M. Anson, *J. Gen. Physiol.* 22, 79 (1938).
6. "Worthington Biochemical Catalog No. 8" (Worthington Biochemical Co., Freehold, N.J., 1957).
7. L. Augenstine, in *Information Theory in Biology*, H. Quastler, Ed. (Univ. of Illinois Press, Urbana, 1953), pp. 119–121; *J. Phys. Chem.* 61, 1385 (1957); in *Information Theory in Biology*, H. Yockey, Ed. (Pergamon, New York, 1956), pp. 287–291.
8. ———, *Information Theory in Biology*, H. Yockey, Ed. (Pergamon, New York, 1956), pp. 103–123.
9. R. Setlow and B. Doyle, *Biochim. et Biophys. Acta* 24, 27 (1957).
10. M. McDonald, *Brit. J. Radiol.* 27, 62 (1954).
11. R. Monier, *Biophys. et Biochim. Acta* 29, 345 (1958).
12. I. Liener, *J. Biol. Chem.* 225, 1061 (1957).
13. Chymotryptic contamination is probably not the explanation of the effects reported here.

* Present address: Division of Biology and Medicine, U.S. Atomic Energy Commission, Washington 25, D.C. The research discussed in this report was carried out under the auspices of the AEC. I gratefully acknowledge the technical assistance and advice of C. Ghiron and the counsel of numerous colleagues.

2 January 1959

Lack of Abnormal Hemoglobins in Alaskan Eskimos, Indians, and Aleuts

Abstract. In an examination of the blood of 708 Eskimos, 200 Aleuts, and 44 Indians in Alaska for abnormal types of hemoglobin, only normal hemoglobin A was detected. It may be concluded that abnormal hemoglobins in these races are rare if they occur at all.

Although hemoglobins other than normal adult hemoglobin A are found with varying frequency in various racial groups (*1*), these genetic variants of hemoglobin have been found primarily among African or Asian populations. Since the Eskimos, Aleuts, and Indians of Alaska may be of Asian origin, we wished to determine whether any abnormal hemoglobins were characteristic of these Alaskan racial groups. The possibility was also considered that the moderate anemia which is prevalent in Eskimos in western Alaska (*2*) might be related to the presence of an abnormal variant of hemoglobin.

Hemoglobin samples from 593 Eskimos from all parts of Alaska and 25 Indians from central Alaska were tested by paper electrophoresis in Veronal buffer (*p*H 8.6), by alkali denaturation (*3*), and for solubility (*4*). Blood cells from 42 of these persons with moderately low hemoglobins were further examined for osmotic fragility, and the absorption spectra of the hemoglobins were measured. No abnormalities were found in any of the tests.

An additional 334 blood samples were sent to the University of Texas (*5*). Of these, 200 were from Aleuts, 115 were from Eskimos, and 19 were from Indians. The hemoglobins were analyzed by

paper electrophoresis, with Veronal buffer (*p*H 8.6) (*6*). Hemoglobin A was the only type detected in these samples (*7*).

EDWARD M. SCOTT
ISABELLE V. GRIFFITH
DALE D. HOSKINS
Arctic Health Research Center, U.S. Public Health Service, Anchorage, Alaska
ROSE G. SCHNEIDER
Tissue Metabolism Research Laboratory, University of Texas, Medical Branch, Galveston

References and Notes

1. W. W. Zuelzer, *Federation Proc.* **16**, 769 (1957).
2. E. M. Scott, R. C. Wright, B. T. Hanan, *J. Nutrition* **55**, 137 (1955).
3. K. Singer, A. I. Chernoff, L. Singer, *Blood* **8**, 386 (1953).
4. H. A. Itano, *Arch. Biochem. Biophys.* **47**, 148 (1953).
5. The samples were sent through the cooperation of Mr. Frank P. Pauls of the Southcentral Regional Laboratory, Alaska Department of Health, Anchorage.
6. R. G. Schneider, *Texas Repts. Biol. and Med.* **14**, 380 (1956).
7. This study was supported by U.S. Public Health Service grant A-780.

13 October 1958

New Method for the Rapid Determination of Lathyrogenic Agents

Abstract. Salamander and toad embryos will develop grossly observable tumors of the notochord if they are placed for 3 or more days in a solution of the lathyrism-producing chemicals beta-aminopropionitrile or aminoacetonitrile. A technique for using tumorigenesis in amphibian embryos as a biological indicator for other lathyrogenic agents is presented.

Rats fed diets containing large amounts of meal prepared from the sweet pea *Lathyrus odoratus* or containing a crystalline factor isolated from *Lathyrus* seeds develop a syndrome known as experimental lathyrism. The skeletal and other mesenchymal tissue changes of the syndrome can also be produced by feeding small amounts of the nitriles beta-aminopropionitrile (BAPN) or aminoacetonitrile (AAN). In amphibians, the changes can be produced by rearing embryonic forms in water containing either the crystalline factor of the *Lathyrus* seed or one of the nitriles. They are characterized by distortions of the limbs and jaws and by tumors of the notochord.

Interest in experimental lathyrism is increasing, probably as a part of the recent general interest in diseases of the connective tissues, and probably because of the similarity between induced lesions in the experimental disease and such human afflictions as slipped epiphyses, degenerative arthritis, and dissecting aortic aneurism (*1*).

Only a few compounds, notably the nitriles, have been shown to produce lathyrism, and the mode of action by which these chemicals produce the lesions has not been explored. Recently Dasler (*2*) has shown that semicarbazide will produce lesions of osteolathyrism in the rat. Since semicarbazide is a known aldehyde blocking agent, it occurred to my coworkers and me that other water-soluble aldehyde blocking agents might also produce lathyrism.

Salamander and toad embryos reared for 3 days in water containing a lathyrogenic nitrile exhibit gross tumors of the notochord. It seemed likely that these animals could be used as a biological screening tool for new lathyrogenic agents.

Ten to 20 embryos of the salamander *Amblystoma punctatum* or of the toad *Bufo americanus* in early tail bud stages were placed in finger bowls containing 100 ml of various concentrations (0.01 to 100 mg/100 ml) of an aldehyde-blocking agent in spring water (Table 1). These agents were selected from chemicals frequently used in blocking the periodic acid-Shiff histochemical reaction. The embryos were examined daily under the dissecting microscope for evidence of tumor formation, which is the first gross sign of lathyrism. The known tumorigenic agents, BAPN and AAN, were used as controls. The experiments were usually terminated after 1 week. All chemicals tested except sodium bisulfite, hydrazine hydrate, and hydroxylamine hydrochloride produced tumors (Table 1) (Fig. 1).

Dasler's (*2*) finding that semicarbazide produced osteolathyrism in rats opened a relatively new field for the investigation of connective tissue metabolism. Dasler pointed out that finding new osteolathyrogenic agents might aid in locating the metabolic defect in the disease. Our technique provides a rapid and accurate screening method for seeking such agents. Our findings suggest that the defect might be concerned with carbohydrate metabolism of the connective tissue ground substance (*3*).

Table 1. Effects of various aldehyde blocking agents on tumor formation in salamander and toad embryos.

Blocking agent	Result	Lowest effective concn. (mg/100 ml)
Amino antipyrine HCl	Tumor	50
Hydrazine hydrate	No tumor	
Phenylhydrazine*	Tumor	1
1-Methyl-1-phenylhydrazine	Tumor	0.5
1-Benzyl-1-phenylhydrazine HCl	Tumor	1
Semicarbazide†	Tumor	1
Thiosemicarbazide	Tumor	10
4-Phenyl-3-thiosemicarbazide	Tumor	3
Hydroxylamine HCl*	No tumor	
Sodium bisulfite†	No tumor	
Urea†	Tumor	1
BAPN	Tumor	1
AAN	Tumor	1

* Baker. † Fisher.

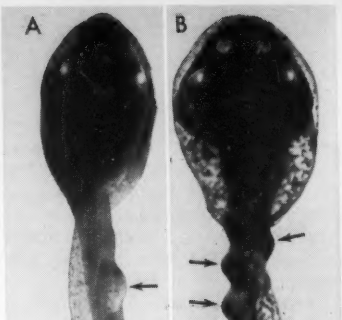


Fig. 1. Single (*A*) and multiple (*B*) tumors in tadpoles after immersion for 1 week in beta-aminopropionitrile.

BARNET M. LEVY
University of Texas Dental Branch, Houston

References and Notes

1. C. Y. Chang, E. Witschi, I. V. Ponseti, *Proc. Soc. Exptl. Biol. Med.* **90**, 45 (1955).
2. W. Dasler, *ibid.* **97**, 112 (1958).
3. The technical assistance of Johnnie Goodrich is gratefully acknowledged. The 1-benzyl-1-phenylhydrazine HCl and the 4-phenyl-3-thiosemicarbazide used in this study were provided through the courtesy of M. S. Burstone of the National Institute of Dental Research. I am indebted to Ulrich Weiss of the National Institutes of Health for the thiosemicarbazide and to Waldeman Dasler of Chicago, Ill., for the beta-aminopropionitrile and the aminoacetonitrile. This investigation was supported in part by grant D-822 from the National Institutes of Health, U.S. Public Health Service.

14 October 1958

Effect of Ultraviolet Light on Pectolytic Enzyme Production and Pathogenicity of Pseudomonas

Abstract. Ultraviolet radiation-induced mutants of the soft rot bacterium *Pseudomonas marginalis* were selected for loss of pathogenicity for lettuce and wildoof chicory. The avirulent mutants differed from the parent pathogen in their inability to synthesize pectolytic enzymes in culture or to ferment sodium pectate or sodium polygalacturonate as the sole carbon source in media.

In his pioneer work in 1909, Jones (*1*) postulated that parasitism in the soft rot bacteria seemed to be associated directly with the ability to produce pec-

tolytic enzymes. This viewpoint has been restated more recently (*2*). As far as can be ascertained from the literature, there appears to be no direct experimental evidence that loss of ability by a soft rot bacterium to produce pectolytic enzymes has resulted in loss of pathogenicity. The purpose of the present communication is to report evidence bearing on this aspect of the host-pathogen relationship.

Pseudomonas marginalis (Brown) Stevens, strain P1 pathogenic for lettuce, was selected for study. The bacterium was isolated originally from witloof chicory (*Cichorium intybus* L.) in 1949 (*3*). Cell-free culture filtrates of the pathogen are now known to cause soft rot, russet spotting, and vascular browning of lettuce and to contain protopectinase (or macerating enzyme complex), pectin depolymerase, and pectinmethylesterase (*4*).

Bacterial suspensions of *P. marginalis* in water were irradiated with ultraviolet light (15-watt General Electric germicidal lamp) at a distance of 22.5 cm for varying periods of time up to 10 minutes. Cells surviving exposure were plated out on yeast extract-nutrient agar, and 17 single-colony isolates were tested for pathogenicity. Ten of these showed complete inability, in repeated tests, to infect leaves of witloof chicory and head lettuce (*Lactuca sativa* L.) following needle inoculations with cells grown on yeast extract-nutrient agar.

Five isolates chosen at random from the ten avirulent isolates failed in repeated tests to produce pectolytic enzymes in cultures of lettuce broth and Uschinsky broth, even though they formed heavy, fluorescent growth in the broths. Under similar conditions the pathogenic P1 strain exhibited protopectinase, depolymerase, and pectinmethylesterase activity. Furthermore, the addition of 0.15-percent Seitz-sterilized pectin to an Uschinsky broth culture of an avirulent isolate (strain M4) failed to induce the formation of pectolytic enzymes. Although the mutants have been in culture over 6 months and have been transferred at approximately biweekly intervals, they have not reverted to a virulent state, and they have not produced pectolytic enzymes in culture.

To ascertain whether the avirulent M4 and the virulent P1 strains differed in other respects, the two were compared morphologically, culturally, and physiologically by means of standard methods (*5*). The strains were found to be similar with respect to characteristics previously reported for P1 (*3*), except for their reactions in synthetic broths containing 0.15- to 0.5-percent sodium pectate or sodium polygalacturonate or 1-percent sucrose as the sole carbon source. The avirulent strain M4 failed to ferment these substances, whereas the virulent P1 strain produced alkali from the pectic substrates and acid from sucrose.

Recently it was reported that ultraviolet irradiation of the soft rot bacterium *Erwinia aroideae* produced some specific nutritional mutants which showed a loss of pathogenicity resulting from the inability of the mutants to find on the host tissue the required nutrilites for growth (*6*). Five avirulent strains and strain P1 of *P. marginalis* were grown in minimal broth and minimal agar to determine whether a nutritional mutation was involved in these cultures also. For this purpose eight different, simple synthetic broths [including Davis and Mingioli broth and Entner and Stanier broth (*7*)] and four agar media were used. Inorganic salts or asparagine were used as nitrogen sources, while sodium acetate, glycerol, dextrose, or asparagine were used as carbon sources. Noble (Difco) or washed agar were used for the solid media. Cells washed with 0.8-percent sodium chloride were used to inoculate the media. In all cases, the growth of the five avirulent strains on the minimal media was comparable to that of the virulent parent strain, indicating that a nutritional mutation was not involved.

It is known that the presence of inhibitory substances in plant tissue may affect the host-pathogen relationship (*8*), but in the present study unheated, blended lettuce extracts did not inhibit the growth of the avirulent M4 strain in culture. In addition, it is recognized that there are saprophytic species of *Pseudomonas* and other microorganisms which are able to form pectolytic enzymes in culture but are unable to invade plant tissue (*9*). In the case of these saprophytes, failure to cause disease must be due to some mechanism other than the inability to produce pectolytic enzymes. Although pectolytic enzymes play a decisive role in soft rots of plants, it is quite possible that other enzymes play some role in pathogenesis by *P. marginalis*. In the present study, however, assays for other enzymes were not made.

In summary, the results in the present study of the soft rot pathogen *P. marginalis* indicate that loss of pathogenicity by the radiation-induced mutants is genetic in nature and is linked with their inability to form pectolytic enzymes and with their consequent inability to attack the pectic substrates present in inoculated host tissues.

B. A. FRIEDMAN
M. J. CEPONIS

Market Pathology Laboratory,
U.S. Department of Agriculture,
New York, New York

References and Notes

1. L. R. Jones, *N.Y. (State) Agr. Expt. Sta. (Geneva, N.Y.) Bull. 11* (1909), part 2, p. 289.
2. W. Brown, *Ann. Appl. Biol.* 43, 325 (1955); A. F. Murant and R. K. S. Wood, *ibid.* 45, 635 (1957).
3. B. A. Friedman, *Phytopathology* 41, 880 (1951).
4. Assay methods for determining the pectolytic enzymes produced by *P. marginalis* are given in a forthcoming article (*Phytopathology*, in press).
5. Society of America Bacteriologists, *Manual of Microbiological Methods* (McGraw-Hill, N.Y., 1957), pp. 37, 140, 169.
6. E. D. Garber, *Proc. Natl. Acad. Sci. U.S.* 40, 1112 (1954).
7. B. D. Davis and E. S. Mingioli, *J. Bacteriol.* 60, 17 (1950); N. Entner and R. Y. Stanier, *ibid.* 62, 181 (1951).
8. J. C. Walker and M. A. Stahmann, *Ann. Rev. Plant Physiol.* 6, 351 (1955).
9. D. H. Lapwood, *Ann. Botany (London)* 21, 167 (1957).

6 October 1958

Intracellular Impulse Conduction in Muscle Cells

Abstract. A hypothesis, suggested previously by morphological studies, for impulse conduction from the sarcolemma to the contractile material via the sarcoplasmic reticulum is discussed. The relation of reticulum morphology and cell size to speed of contraction in smooth and striated muscle agrees with the hypothesis and thus supports it. Additional support comes from evidence concerning an unusual morphological relationship between the sarcolemma and contractile fibrils in striated muscle of amphioxus.

Studies of the fine structure of cells by recently developed physical means, such as electron microscopy, have stimulated the formulation and study of hypotheses of the mechanisms of various cellular functions. The worth and durability of these hypotheses will depend ultimately, of course, on sound physiological demonstration that the mechanisms are in reality those described by the hypotheses. It is valuable in the meantime, however, to formulate hypotheses, provided that they suggest new lines of experimental investigation. Such investigation, when carried out, will lead to validation or rejection of the hypothesis.

It is the purpose of this report to discuss a hypothesis of intracellular impulse conduction in muscle cells that has been suggested by cytological observations recently made with the electron microscope. As is shown, the hypothesis is justified in that it brings the previously paradoxical time-distance relationships in muscle into proper order and suggests investigation directed toward the demonstration of the presence of intracellular membrane potentials and depolarization phenomena.

The paradox referred to is as follows: Striated muscle cells, which average 50 to 100 μ in diameter, contract very quickly and across the entire diameter of the cell very soon after the action potential has passed over the cell membrane. Smooth muscle cells, on the other hand, which average 6 to 10 μ in diameter, contract slowly, and parts of the cell come into play only at relatively long

times after the cell membrane action potential has passed. It is immediately obvious that the relationship between cell size and delay time is reversed from what one would expect if the contraction-inducing impulse were to pass from the cell surface to the contractile elements by the same mechanism in each case, and if, of course, the other events, such as the activation of the contractile material, required the same time in both striated muscle cells and smooth muscle cells. This forms the paradox referred to above.

The possibility of the diffusion of a substance from the cell surface toward the central axis of the cell has been considered by Hill as a possible mechanism of impulse transfer (*1*). Hill shows, however, that diffusion would be too slow to account for the rapid sequence of events in striated muscle cells (*2*). This does not, however, rule out the possibility that this mechanism could act in smooth muscle cells. Indeed, the paradox suggests that the over-all mechanism is not the same in striated and smooth muscle cells, and our calculations show that diffusion times over distance of the order of the radii of smooth muscle cells (3 to 5 μ) fall well within the limit of observed delay times for smooth muscle. The problem then becomes one of finding an alternate mechanism which is coupled to both the cell surface and the contractile elements and which is fast enough to account for the short delay time in striated muscle.

The mechanism discussed here is based on electron-microscope studies of striated muscles of several types (*3–5*) that rediscovered a system of the sarcoplasm which presumably corresponds to a system described in light microscope images by Thin in 1874 (*6*).

The major characteristics of this system, called the "sarcoplasmic reticulum," are that it is a continuous, membrane-limited, reticular system whose structural organization repeats longitudinally and synchronously in parallel with the bands which form the sarcomeres, and which is continuous laterally between the fibrils across the whole diameter of the cell. It is closely associated with the external membrane of the cell on the one hand, and with the myofibrils on the other. Indeed, the latter association is characterized in vertebrate skeletal muscle by a special differentiation opposite the I-band level of each sarcomere, where contraction presumably is initiated (*7*), and points to a probable role in the contractile function of the cell.

It has occurred to several authors, in discussing the sarcoplasmic reticulum (*3, 5, 8*), that it is possible that this system could serve to transmit the excitatory impulse intracellularly. One possibility is that the membranes forming the sarcoplasmic reticulum are electrically polarized in a manner similar to the polarization of the muscle and the external membrane of the nerve cell. Since the sarcoplasmic reticulum divides the sarcoplasm into two compartments which communicate only *through* a membrane, it seems likely that the two phases thus delineated differ in type or activity of chemical species, or in both, and therefore the presence of a chemical and electrical potential gradient seems not only possible, but probable.

Assuming this to be true, we can further propose that the polarized membrane is capable of conducting an impulse, and that this conduction is coupled to the depolarization of the cell external membrane by its close proximity to the latter and to the contractile elements by diffusion of an activating substance over relatively short distances. Thus we have postulated the existence of a new *excitable unit* at the level of the fibril and even at the level of certain sensitive sections of the fibril. This changes the diffusion distance in striated muscle, which corresponds to the diffusion distance of 3 to 5 μ in smooth muscle, from 25 to 50 μ, which is the radius of the striated muscle *cell,* to 0.5 to 1.0 μ, which is the radius of the striated muscle *fibril.* The time-distance paradox is thereby resolved, and the possibility that a diffusion mechanism of activation of contraction applicable to both striated and smooth muscle is once more admissible.

The hypothesis has been able to explain previously inexplicable data. It now remains to examine the validity of the hypothesis both by examining its implications in the light of available data, and with experimental tests suggested by the hypothesis.

We can determine the effect the new hypothesis, which was derived from considerations of striated muscle, will have on our picture of time-distance relationships in smooth muscle. Examination of smooth muscle cells in the electron microscope reveals the presence of only a small complement of sarcoplasmic reticulum (*9*). There certainly appears to be no massive, well-developed system such as has been seen in most striated muscle cells thus far examined. Thus, the excitable membrane in smooth muscle would seem to remain the external membrane of the cell. This consideration, therefore, strengthens the hypothesis.

We can deduce from the hypothesis that the speed of contraction should increase as the size of the excitable unit decreases. This has been found to be the case for the limited data available at present, which concern only the difference between the two major classifications of muscle cells, smooth and striated. That is to say, most striated muscle cells examined have been from fast muscles and have had well-developed reticula surrounding small fibrils, while no smooth muscle has been found with such a well-developed reticulum, leaving the relatively large single cell as the excitable unit in this type of muscle. A more careful correlation of size of the excitable unit and the speed of contraction for various muscles within each of the major classifications is planned. This correlation will help to evaluate the validity of the hypothesis. There is supporting evidence at present, however, from some work by one of us (L.D.P.) on the myotomes of the primitive chordate amphioxus (*Branchiostoma carribbaeum*). These muscles are fast, judging from the quick swimming motion of the animal, but do not have a well-developed reticulum. The myofibrils are, however, in the form of flat sheets or lamina about 1 μ thick, and both large faces of each fibril are closely associated with the external membrane of the cell, which completely covers each of the flat fibrils. Thus the action potential is carried directly by the cell membrane to within 0.5 μ of the center of the fibril, and the time-distance relationship becomes approximately the same as that for striated muscle cells with cylindrical fibrils of this size sheathed in sarcoplasmic reticulum.

Other lines of investigation which are presently being carried out involve determination of the effect of changes in intracellular ionic concentrations on the morphology of the reticulum, with correlation of the reticulum morphology with the functional state of the muscle cell, and an investigation of the morphology of muscle cells from a wide variety of species with particular attention to the spatial relationships of the cell membrane, the sarcoplasmic reticulum, and the contractile material. We hope that information will soon be available which will allow a more critical evaluation of the hypothesis discussed here than is presently possible.

LEE D. PEACHEY
KEITH R. PORTER
Rockefeller Institute, New York

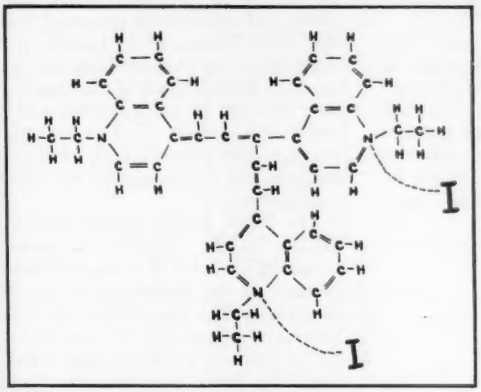
References and Notes

1. A. V. Hill, *Proc. Roy Soc.* (*London*) **B135**, 446 (1948).
2. ———, *ibid.* **B136**, 399 (1949).
3. H. S. Bennett and K. R. Porter, *Am. J. Anat.* **93**, 61 (1953).
4. G. A. Edwards and H. Ruska, *Quart. J. Microscop. Sci.* **96**, 151 (1955).
5. G. A. Edwards, H. Ruska, P. Souza Santos, A. Vallejo-Freire, *J. Biophys. Biochem. Cytol.* **2**, No. 4, suppl. 143 (1956); K. R. Porter, *ibid.* **2**, No. 4, suppl. 163 (1956); K. R. Porter and G. E. Palade, *ibid.* **3**, 269 (1957).
6. G. Thin, *Edinburgh Med. J.* **20**, pt. 1, 238 (1874).
7. A. F. Huxley and R. E. Taylor, *J. Physiol.* (*London*) **130**, 49P (1955).
8. G. Retzius, *Biol. Untersuch.* **1**, 1 (1881).
9. J. S. T. Mark, *Anat. Record* **125**, 473 (1956).

21 February 1958

Kodak reports on:

trapping photons and transferring their energy . . . a film that separates the lemons from the oranges . . . what's good for the missileers is good for the chromatographers



Old model resonator

Look—with the eye of a quantum mechanic—at this marvelous little molecular resonating machine. For the trifling sum of $16.65 we can supply 400 quintillion of these machines. They will weigh ½ gram, all told, and will come in a small bottle labeled *Neocyanine* (Eastman 2067).

The two iodines come separately packed in the crystal lattice as ions. The points where they were detached, at the quaternary nitrogens, are positively charged, of course. Either of these two positive charges can be sent skittering back and forth through the branched chain of conjugated carbon atoms to bounce off the third nitrogen atom. All it takes to set the machine resonating thus is a photon of light or infrared that carries the difference in energy between quiescence of the positive charges and resonance thereof.

This little resonator has proved useful for trapping photons and transferring their energy to silver halide crystals. The silver halide thereupon responds photographically to wavelengths it would otherwise miss.

This is a 1925 model. We have since devised thousands of more advanced models of this basic type of resonator, but stock only the above and five other simple ones for off-the-shelf delivery: *Cryptocyanine* (Eastman 1334), *Dicyanine A* (Eastman 1532), *Pinacyanole* (Eastman 622), *Pinaflavole* (Eastman 1842), and *Orthochrome T* (Eastman 623). As dyes they are exceedingly powerful.

For a discussion of the working parts from which such ultra-subminiaturized electronic machines can be built by the skillful worker, see a paper entitled "A Century of Progress in the Synthesis of Dyes for Photography." As long as our supply of reprints lasts, we can send you a copy free.

Write to Distillation Products Industries, Eastman Organic Chemicals Department, Rochester 3, N. Y. (Division of Eastman Kodak Company). The latest catalog, No. 41, also lists some 3700 other compounds for research.

Process E-3

Distinguished by the designation "(Process E-3)" from earlier versions, a new *Kodak Ektachrome Film* is aimed to please the worker who is pretty all-fired sure that for any trifling deficiency in his color transparencies the fault has lain not in himself, not in his technique, not in his equipment, but in his film.

Beyond the shadow of an illusion, this film is *sharper* than its predecessors. *Sharpness* differs from contrast and from resolving power. It represents ability to render a boundary—within how few microns the color on the transparency can change from (let us say) a certain yellow to a certain orange. This ability does not readily lend itself to quantitative statement.

We mention yellow and orange advisedly. A classic challenge to any color photographic process has been to distinguish between the hue of lemons and oranges in one bowl of fruit. The new film meets it handily. Greens are better, too.

More valuable to some users will be the fidelity of the new film to the visual appearance of such photographically elusive biological stains as eosin and fuchsin. The photomicrographer now gets not only an enhancement of the fine color discrimination for which *Ektachrome* was notable even before but a new advantage in speed. Exposure Index is 32 for the *Type B* (which requires only heat-absorbing and possibly U-V filters in the usual photomicrographic setups) and 50 for the *Daylight Type* (used with electronic flash). Statistics show that in 1/25 second you get only 20% of the vibration contained in 1/5 second.

Kodak dealers now stock the new Kodak Ektachrome Film (Process E-3) *in the usual sheet-film sizes. For 120 and 620 roll-film cameras it's called* Kodak Ektachrome Professional Film, Daylight Type (Process E-3). *They also carry various-sized kits of the new processing chemicals that Process E-3 requires. The processing cycle takes about an hour.*

If a) you want paper prints and duplicate transparencies, and if b) you want to be able to manipulate your color balance toward a conception of reality transcending what can be built into inanimate film, and if c) you are willing to process both a negative and a positive before you judge your results, don't even bother with this new stuff. Stick to Kodak Ektacolor Film and Paper.

See the steroid?

When we brought out *Kodak Linagraph Direct Print Paper* we never dreamed of steroids. We were dreaming of the long, long miles of galvanometer data traces that the missileers would be happy to make on a photographic paper requiring no wet processing.

These dreams having come true, correspondence on the product is handled by gentlemen who don't even know what a steroid is. Of the inconvenience in locating on a paper chromatogram a substance readily discernible only by its ultraviolet absorption, they know even less. They have never read pp. 255-305 in Volume 7 of "Recent Progress in Hormone Research" (Academic Press, New York, 1952).

Fortunately, biochemical laboratory technique need not be discussed with them. A short paper in *Analytical Chemistry* (*12, 2068*) describes how a piece of Kodak Linagraph Direct Print Paper, briefly exposed to an ultraviolet lamp while kept in good contact under a dried chromatogram, will upon subsequent exposure to a 30-watt fluorescent lamp show light gray areas against a dark background at the sites of U-V absorbers in the chromatogram. The method is reported successful in routine use where 5γ or more is present of the absorber per square centimeter of paper.

To find out where to order Kodak Linagraph Direct Print Paper, *write Eastman Kodak Company, Photo-recording Methods Division, Rochester 4, N. Y. That much they know.*

Kodak
TRADE MARK

This is another advertisement where Eastman Kodak Company probes at random for mutual interests and occasionally a little revenue from those whose work has something to do with science

Meetings

Biological Exhibits at Geneva

The second International Conference on the Peaceful Uses of Atomic Energy, held in Geneva, Switzerland, 1–13 September, was participated in by many countries as guests of the United Nations. The basic objective of the United States was to provide, wherever possible, operating laboratories and exhibits staffed with scientists skilled in various areas of research. An integrated picture of nuclear research was presented, which included power, physics, chemistry, and the life sciences. Many people availed themselves of the opportunity provided for discussion, and the American exhibit became a meeting ground for scientists from around the world.

Short-lived radioisotopes were prepared in a Triga reactor and utilized in an activated isotope laboratory operated by personnel from the National Naval Medical Center. Drugs and biochemically important compounds were labeled with C^{14}, S^{35}, and H^3 and assayed in a chemistry laboratory operated by the Chemistry Division of the Argonne National Laboratory and the University of Chicago's department of pharmacology. Biosynthetic labeling was demonstrated in a greenhouse transported from the Argonne National Laboratory and operated by personnel from the biology division of the laboratory. A large display on phytosynthesis was prepared by the University of California, as were exhibits on erythropoietin and a gamma-ray camera used in medical practice. The Roswell Park Memorial Institute sent a photoscanner for tumor localization.

The Public Health Service provided exhibits on the diagnosis of cardiac anomalies by means of radioactive noble gas and on the metabolism of labeled carcinogens. The Los Alamos Scientific Laboratory operated a "Human Counter," which was a very popular attraction. The Army Quartermaster Corps developed an exhibit on food preservation, and the Department of Agriculture exhibit on parasite eradication was especially attractive. The universities of Maryland, Illinois, and California cooperated to develop an exhibit on milk synthesis. The measurement of C^{14}-labeled lysergic acid diethylamide in brain was displayed by the University of Rochester. The biodynamics of $C^{14}O_2$ was demonstrated in patients by a group from the University of Chicago, who also demonstrated the technique of hypophysis ablation, using yttrium-90 implants. New developments in the field of autoradiography were displayed in exhibits from Columbia University and the universities of Arkansas and Chicago.

LLOYD J. ROTH
University of Chicago, Chicago, Illinois

JOHN H. RUST
Massachusetts Institute of Technology, Cambridge, Mass.

Differential Equations

A Symposium on Boundary Problems in Differential Equations, with special reference to recent developments in this field, will be held by the Mathematics Research Center, U.S. Army, at the University of Wisconsin, 20–22 April. Invited speakers, about 20 in number, will each present a 30-minute paper. Both ordinary and partial differental equations will be considered, the emphasis to be upon methods that are potentially adapted to computation. The proceedings of the symposium will be published.

Among the speakers, European and American, will be L. Collatz, G. Fichera, L. Fox, W. T. Koiter, J. Schröder, I. N. Sneddon, R. Bellman, G. Birkhof, H. Bueckner, R. Courant, J. B. Diaz, J. Douglas, K. Friedrichs, P. Garabedian, B. A. Troesch, R. Varga, C. Wilcox, and

D. Young. Persons interested in attending the symposium may obtain the program and other details from R. E. Langer, Director, Mathematics Research Center, U.S. Army, 1118 West Johnson St., Madison 6, Wis.

Molecular Structure

A Symposium on Molecular Structure and Spectroscopy will be held at the department of physics and astronomy, Ohio State University, 15–19 June. There will be discussions of the interpretation of molecular spectroscopy data as well as of methods for obtaining such data. In addition, there will be special sessions on phases of spectroscopy that are of current interest. A dormitory will be available for those who wish to reside on the campus during the meeting. For further information, or for a copy of the program when it becomes available, write to Professor R. A. Oetjen, Department of Physics and Astronomy, Ohio State University, Columbus 10, Ohio.

Data Processing

The Denver Research Institute of the University of Denver will hold its 6th annual Symposium on Computers and Data Processing at the Stanley Hotel in Estes Park, Colo., 30–31 July. The conference will be restricted to papers and panel discussions on basic problems in the fields of data processing, particularly in the area of formalized analysis techniques, logical design, systems organization, and components or devices.

Although it is anticipated that the program will be comprised largely of invited papers, a limited number will be selected from those submitted to the papers committee. Authors wishing to present papers are urged to send abstracts of approximately 150 words, *no later than 1 April,* to: W. H. Eichelberger, Papers Committee, Denver Research Institute, University of Denver, Denver 10, Colo.

Forthcoming Events

April

11. Extending the Parabola, Alfred Korzybski Memorial Symp., New York, N.Y. (E. L. Gates, Inst. of General Semantics, Lakeville, Conn.)

12–14. Atomic Mechanisms of Fracture, conf., Cambridge, Mass. (D. K. Felbeck, Natl. Acad. of Sciences–Natl. Research Council, 2101 Constitution Ave., NW, Washington 25.)

12–15. Neurosurgery, 8th Latin American cong., Santiago, Chile. (A. Asenjo G., Casilla 70-D, Santiago, Chile.)

12–16. American Physiological Soc., Atlantic City, N.J. (R. C. Daggs, 9650 Wisconsin Ave., Washington, D.C.)

12–16. Fracture, intern. conf., Cambridge and Dedham, Mass. (Headquarters, Air Force Office of Scientific Research, Washington 25.)

13. Biochemical Cytology of Liver (Histochemical Soc.), symp., Atlantic City, N.J. (A. B. Novikoff, Dept. of Pathology, Albert Einstein College of Medicine, Yeshiva Univ., Eastchester Rd. and Morris Ave., New York 61.)

13–15. Hydraulics Conf. (American Soc. of Mechanical Engineers), Ann Arbor, Mich. (O. B. Schier, ASME, 29 W. 39 St., New York 18.)

13–17. American Assoc. of Immunologists, Atlantic City, N.J. (C. Howe, 630 W. 168 St., New York 32.)

13–17. American Inst. of Nutrition, Atlantic City, N.J. (G. M. Briggs, NIAMD, Room 9D20, Bldg. 10, National Institutes of Health, Bethesda, Md.)

13–17. American Soc. for Pharmacology and Experimental Therapeutics, Atlantic City, N.J. (H. Hodge, Univ. of Rochester, Rochester 20, N.Y.)

13–18. American Acad. of Neurology, Los Angeles, Calif. (J. M. Foley, Boston City Hospital, Boston, Mass.)

13–18. American Soc. of Biological Chemists, Atlantic City, N.J. (F. W. Putnam, Univ. of Florida Medical School, Gainesville.)

13–18. American Soc. for Experimental Pathology, Atlantic City, N.J. (J. F. A. McManus, Univ. of Alabama Medical Center, Birmingham 3.)

14–15. Electrical Heating Conf. (American Institute of Electrical Engineers), Philadelphia, Pa. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

14–16. Faraday Soc. (Energy Transfer), Nottingham, England. (Faraday Soc., 6 Gray's Inn Square, London, W.C.1, England.)

14–16. Life Span of Animals, 5th colloquium on aging, London, England.

(Ciba Foundation, 41 Portland Pl., London, W.1.)

14–16. Rheology of the Glassy State (British Soc. of Rheology), Sheffield, England. (D. W. Saunders, British Rayon Research Assoc., Heald Green Laboratories, Wythenshawe, Manchester 22, England.)

15–17. American Assoc. of Genito-Urinary Surgeons, Absecon, N.J. (W. J. Engel, 2020 E. 93 St., Cleveland 6, Ohio.)

15–17. American Surgical Assoc., San Francisco, Calif. (W. A. Altemeier, Cincinnati General Hospital, Cincinnati 29.)

15–17. Midwest Benthological Soc., annual, Hickory Corners, Mich. (C. M. Fetterolg, Jr., Water Resources Commission, Sta. B, Lansing 13, Mich.)

16–18. American Assoc. of Railway Surgeons, Chicago, Ill. (C. C. Guy, 5800 Stony Island Ave., Chicago 37.)

16–18. Association of Southeastern Biologists, Knoxville, Tenn. (H. J. Humm, Dept. of Botany, Duke Univ., Durham, N.C.)

16–18. Ohio Acad. of Sciences, Columbus. (G. W. Burns, Ohio Wesleyan Univ., Delaware.)

16–18. Southern Sociological Soc., 22nd annual, Gatlinburg, Tenn. (S. C. Mayo, North Carolina State College, Raleigh.)

16–30. Engineering, Marine, Welding and Nuclear Energy Exhibition, 22nd, Olympia, London. (F. W. Bridges & Sons, Ltd., Grand Buildings, Trafalgar Square, London, W.C.2, England.)

17. Current Developments in the Production of High Vacua, symp., London. England. (Institute of Physics, 47 Belgrave Square, London, S.W.1.)

17–18. American Mathematical Soc., Monterey, Calif. (E. G. Begle, Leet Oliver Hall, Yale Univ., New Haven, Conn.)

17–18. American Mathematical Soc., Chicago, Ill. (E. G. Begle, Leet Oliver Hall, Yale Univ., New Haven, Conn.)

17–18. Nebraska Acad. of Sciences, 69th annual, Lincoln. (M. Beckman, Teachers College, Univ. of Nebraska, Lincoln.)

18–19. Myasthenia Gravis, 2nd intern. symp., Los Angeles, Calif. (K. E. Osserman, Myasthenia Gravis Foundation, Inc., 155 E. 23 St., New York 10.)

18–22. American Soc. of Tool Engineers, 27th annual, Milwaukee, Wis. (ASTE, 10700 Puritan, Detroit 38, Mich.)

19–23. Oil and Gas Power Conf. (American Soc. of Mechanical Engineers), Houston, Tex. (O. B. Schier, ASME, 29 W. 39 St., New York 18.)

19–24. American Pharmaceutical Assoc., annual conv., Cincinnati, Ohio. (R. P. Fischelis, APA, 2215 Constitution Ave., Washington 7.)

20–21. Analog and Digital Instrumentation, 3rd natl. conf. (American Inst. of Electrical Engineers), Philadelphia, Pa. (N. S. Hibshman, AIEE, 33 West 39 St., New York 18.)

20–22. American Oil Chemists' Soc., spring, 50th anniversary, New Orleans, La. (Mrs. L. R. Hawkins, 35 E. Wacker Dr., Chicago 1, Ill.)

20–22. Boundary Problems in Differential Equations, symp., Madison, Wis. (R. E. Langer, Mathematics Research Center, U.S. Army, 1118 W. Johnson St., Madison 6.)

(See issue of 20 February for comprehensive list)

Equipment

The information reported here is obtained from manufacturers and from other sources considered to be reliable, and it reflects the claims of the manufacturer or other source. Neither Science *nor the writer assumes responsibility for the accuracy of the information. A coupon for use in making inquiries concerning the items listed appears on page 734.*

■ VOLTAGE-CURRENT CALIBRATOR delivers continuously variable positive or negative voltages from 1 mv to 100 v in four ranges. The output is available either as a direct voltage or as a 5-msec pulse repeated from 5 to 50 times per second. Currents are calibrated by voltage drop produced across an internal 1-ohm resistor. Accuracy is ± 0.3 percent. (Rese Engineering, Inc., Dept. 682)

■ X-RAY IMAGE INTENSIFIER offers binocular viewing of the image of a 5-in. field intensified 1000 times. The device is compact enough to permit normal access to the fluoroscopic mechanism and can be connected or disconnected by means of a quick-release clamp. (Keleket X-Ray Corp., Dept. 680)

■ SOLID-STATE ELECTRONIC COMMUTATOR will sample up to a maximum of 1000 channels of information at rates up to 100,000 samples per second. Accuracy of the switches is a function of the full scale of the signals being commutated. For example, a full scale of ±1 v would have a total error of 0.07 percent, ± 8 v full scale would have a total error of 0.02 percent. (Packard-Bell Computer Corp., Dept. 685)

■ MERCURY BATTERY PACKS are designed for use as secondary voltage standards. Desired voltages can be made up by combination of basic cells of nominal open-circuit voltage 1.357 ± 0.5 percent. Voltage declines 1 percent in 2 years' storage at 70°F. Short-period stability of 1 part in 10,000 is obtainable. Voltage remains stable within ±1 percent over a temperature range – 40° to 160°F. (Mallory Battery Co., Dept. 686)

■ DELAYED-PULSE GENERATOR is adjustable in 1-μsec steps from 1 to 10,000 μsec with provision for interpolation between steps. Over-all accuracy is within ±0.1 μsec, and jitter is less than 0.02 μsec. Time intervals may be initiated internally at rates from 10 cy to 10 kcy/sec or by external signals from 0 to 10 kcy/sec. (Hewlett-Packard Co., Dept. 689)

■ ZONE REFINER applies the zone melting principle to the purification of organic compounds or other materials that melt between 50° and 300°C. The material to be purified is contained in a glass tube. A Nichrome ribbon loop encircles the tube and generates heat to melt the material. As a carriage moves the heater along the tube, the molten zone moves with it. An air-blast ring carried behind the heater cools the tube to solidify the molten material. A second heater and air-blast ring may be used to double the effect of each pass. Zone widths from about ¼ to 2 in. can be obtained by adjustment of the relative position of the heaters and air blast. Carriage motion is adjustable between 0.1 and 2.4 in./hr. (Fisher Scientific Co., Dept. 692)

■ SERVO MILLIVOLTMETER is available as either a ratio meter or an absolute voltage measuring device for full-scale inputs as low as ±5 mv. Accuracy of a standard model is ±0.5 percent, but accuracies as high as ± 0.03 percent can be provided. Visual display and a variety of electrical outputs, analog or digital, are available. (North Atlantic Industries, Inc., Dept. 695)

■ VIBRATION GENERATOR produces double amplitudes up to 1-in. at frequencies from 2 to 20 cy/sec. Table motion is linear in a vertical plane. Specimens weighing 25 lb can be accelerated up to 20 *g*. Frequency may be adjusted while the machine is running. (L. A. B. Corporation, Dept. 687)

■ OXYGEN ANALYZER is available in single or multiple ranges from 0 to 10 parts per million to 0 to 1 percent oxygen. Accuracy is ±2 percent of full scale. A built-in calibrator adds a known amount of oxygen to the sample by electrolysis of water. The analyzer uses an electrochemical cell in which oxygen is catalytically converted at the cathode to hydroxyl ions. The current required is measured by a potentiometer recorder. The instrument responds 90 percent in less than 1 min. (Analytic Systems Co., Dept. 694)

■ SQUIB-ACTUATED MOTOR measures 0.3 in. in diameter by 0.5 in. long and is capable of providing 8 lb of thrust over a 0.1-in. minimum stroke within an elapsed time of 1 msec. The motor is actuated by as little as 7500 erg and will withstand accelerations of 20,000 *g*. Operating temperature range is – 65° to + 165°F. (Atlas Powder Co., Dept. 691)

■ PLUG-IN VOLTMETER CIRCUITRY contains complete vacuum-tube voltmeter circuitry but does not include meter, calibration control, zero adjust, or input voltage divider. With this unit meters being utilized for other purposes may also be used for voltage measurement in the range 1 to 1000 v. Input resistance is 10 megohm. The circuit requires a meter of sensitivity 50 to 250 μa. (Metronix, Inc., Dept. 688)

JOSHUA STERN

National Bureau of Standards, Washington, D.C.

Letters

(Continued from page 684)

wide range of concentrations may be used, and some popular modifications of the Gram stain employ crystal violet near this concentration—for example, Nicolle's (0.33 percent) (*2*). At relatively higher concentrations (1 to 2 percent), the bacteria clump and the dye polymerizes, causing uncertainties in the interpretation of work of this and similar types.

The work of Fischer (*3*) and of Fischer and Zaleschuk (*4*) deals with a method of measurement of crystal violet taken up by various biological materials. This is applicable to the Gram reaction only if one accepts Fischer's statement that "gram positiveness is related to the amount of primary dye absorbed" (*3*). This is not necessarily "conclusively demonstrated," since other studies have shown that crystal violet uptake by bacterial cells is not correlated with their Gram character (*5*). As a matter of fact, the precise and extensive data presented by Wensinck and Boevé (*6*), as cited above by Fischer, indicate that at a dye concentration of about 0.1 percent, a "differential in crystal violet uptake between a Gram-positive and a Gram-negative organism ceases to exist." Since I have shown that Gram differentiation readily occurs when dye of this concentration is used, it appears that measurement of dye uptake does not suffice as a measure of Gram positiveness. The Gram differentiation seems to depend more upon the integrity of the cell membrane or membranes and the relative permeabilities of these membranes to the decolorizing solvent (*6, 7*).

TOD MITTWER
Bacteriology Department, University of Southern California, Los Angeles

References

1. H. Finkelstein and J. W. Bartholomew, *Stain Technol.* 28, 177 (1952).
2. Society of American Bacteriologists, *Manual of Microbiological Methods* (McGraw-Hill, New York, 1957), p. 14.
3. R. Fischer, *Naturwissenschaften* 45, 287 (1958).
4. R. Fischer and J. Zaleschuk, *J. Histochem. and Cytochem.* 6, 237 (1958).
5. J. W. Bartholomew and H. Finkelstein, *J. Bacteriol.* 67, 689 (1954); H. Finkelstein and J. W. Bartholomew, *ibid.* 72, 340 (1956).
6. F. Wensinck and J. J. Boevé, *J. Gen. Microbiol.* 17, 401 (1957).
7. V. Burke and M. W. Barnes, *J. Bacteriol.* 18, 69 (1929).

Echo Ranging in the Porpoise

W. N. Kellogg's paper "Echo ranging in the porpoise," which appeared in a recent issue of *Science* [**128**, 982 (1958)], causes me to wonder about the efficacy of the journal's referee system (or that part of the editorial procedure used instead).

To my knowledge, echolocation in a marine animal was experimentally "demonstrated for the first time" by W. E. Schevill and B. Lawrence of Harvard University and the Woods Hole Oceanographic Institution. Their paper, "Food-finding by a captive porpoise (*Tursiops truncatus*)," appeared as No. 53 of *Breviora* in April 1956 and is discussed at some length in one piece of literature Kellogg cites (Donald R. Griffin's *Listening in the Dark*).

RICHARD H. BACKUS
Woods Hole Oceanographic Institution, Woods Hole, Massachusetts

I am sorry about the omission of a reference to the Schevill and Lawrence paper (*1*) from my recent article in *Science*. The omission was entirely my responsibility and not that of the editors of *Science*. It would have been better to have included it. However, whether the *Breviora* article actually "demonstrates" anything is a matter of opinion. In a way it is regrettable that Backus has raised the issue, for this leaves me no alternative but to point out why the *Breviora* paper fails to prove echolocation, and consequently why the omission was not really a serious one.

It is a basic rule of good research that the variables involved must be properly controlled. This becomes particularly important in a difficult field involving a unique perceptual avenue like echolocation. Under these circumstances we are quite unable to see how leaning over the side of a small boat and feeding fishes to a porpoise by hand can be construed as "demonstrating echolocation." Of course Schevill's porpoise found the fish which he offered, as the title of his article indicates, but from the descriptions given it is impossible to tell what method the porpoise employed to locate the bait. Almost any animal—marine or otherwise—will seek and find food which is near it.

To determine whether a porpoise reacts to the echoes of its own noises, one should certainly not introduce extraneous auditory signals which might help guide the animal to its goal. Slapping the water upon the insertion of the fish—a practice followed in a good deal of the work reported in the *Breviora* article—is the very thing not to do. It simply confuses the issue by telling the animal where (or where not) to go.

Even more serious is the failure to eliminate crucial visual stimuli. Not only can porpoises see through the water and in the air, but they also view objects in the air from a swimming position beneath the surface of the water. Since no visual screening was employed in the *Breviora* study, there would seem to be no reason why the animal could not have observed the movements and postures of

the feeder or feeders, silhouetted against the sky over the side of the boat, on every trial which was made. Having one feeder hold a fish while a second held nothing fails to solve this problem. Unknown and unsuspected optical stimuli may always have been present. The only adequate solution is complete screening to eliminate entirely the human observers as sources of uncontrolled visual cues. Research in comparative psychology has many times demonstrated this fundamental principle (*2*).

The porpoise in the *Breviora* study—even with poor eyesight—may therefore have located its fish (i) by watching the experimenters from beneath the water and noting the position of their bodies, arms, and hands; (ii) by orienting (in some cases) to the sound of the surface splash; or (iii) by echolocation; or by a combination of these methods. The methods of investigation employed, it would appear, do not permit us to say in just what way the animal discovered the fish. When possibilities other than echolocation remain uncontrolled, then echolocation has not been demonstrated to exist as a primary causal factor.

Perhaps the best that can be said of the *Breviora* evidence is that it is inferential. Other inferential evidence, which may be less questionable, was furnished by Kohler, Morris, and me in 1953 (*3*), when we obtained recordings of the actual echoes from porpoise noises and measured the duration of some of these echoes. In fact, I discussed echolocation in the porpoise as a possibility as far back as 1952 (*4*). It should be noted in this connection that two separate papers by Schevill and Lawrence concerning their earlier work with a different porpoise state clearly that "we never heard any sound from her [the porpoise] that could be in any way related to her navigation or food-getting" (*5*), and another states that there was "a complete lack of any evidence that she was using echolocation" (*6*). The most recent of these statements appeared in print in 1954.

It is gratifying to observe that these authors have finally conquered their long-time determination to ride the wrong horse and are now trying to get up on the right one.

W. N. KELLOGG

Department of Psychology,
Florida State University, Tallahassee

References

1. W. E. Schevill and B. Lawrence, *Breviora*, No. 53, 1 (1956).
2. See, for example, J. B. Watson, *Behavior, An Introduction to Comparative Psychology* (Holt, New York, 1914), pp. 300 ff.; also K. S. Lashley, *Psychol. Bull.* 37, 237 (1940).
3. W. N. Kellogg, R. Kohler, H. N. Morris, *Science* 117, 239 (1953).
4. W. N. Kellogg and R. Kohler, *ibid.* 116, 250 (1952).
5. W. E. Schevill and B. Lawrence, *J. Acoust. Soc. Am.* 25, 1016 (1953); *J. Expt. Zool.* 124, 147 (1953).
6. ———, *J. Mammal.* 35, 225 (1954).

PERSONNEL PLACEMENT

CLASSIFIED: 25¢ per word, minimum charge $4.25. Use of Box Number counts as 10 additional words. Payment in advance is required.

COPY for classified ads must reach SCIENCE 2 weeks before date of issue (Friday of every week).

DISPLAY: Rates listed below—no charge for Box number. Monthly invoices will be sent on a charge account basis — provided that satisfactory credit is established.

Single insertion	**$26.00 per inch**
13 times in 1 year	**24.00 per inch**
26 times in 1 year	**23.00 per inch**
52 times in 1 year	**22.00 per inch**

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

Replies to blind ads should be addressed as follows:
Box (give number)
Science
1515 Massachusetts Ave., NW
Washington 5, D.C.

POSITIONS WANTED

Bacteriologist-Biochemist, Ph.D. Varied research experience; bacterial metabolism, lipids, radioisotopes; publications. NSF research fellow, NRC research associate. Desires position, preferably academic. Box 51, SCIENCE. X

Biochemist-Microbiologist, Ph.D. Married, family, veteran, age 31. Experience: Analytical methods, intermediary metabolism of microorganisms, industrial experience. Desires responsible position in industry or teaching position with an opportunity for research. Box 57, SCIENCE. X

Biochemist, Ph.D., 36; protein chemistry and endocrinology. Desires to relocate on West Coast (excluding Los Angeles). Teaching and extensive independent research experience. Box 41, SCIENCE. 3/13

Botanist-Biologist, 45; Cornell Ph.D., 1951; 8 years' experience in southern state university: botany, general biology, plant taxonomy, ecology; AEC research contracts: floristics, ecology, isotopes. Publications. Box 52, SCIENCE. X

M.D., Ph.D. (physiology), 32. American, married, now completing internship, desires career in postclinical investigation. Broad interests; would enjoy some teaching. No military obligations. Box 56, SCIENCE. 3/20, 27; 4/3

Microbiologist, Ph.D.; biochemistry minor. Publications, experience. Desires teaching-research position. Box 55, SCIENCE. X

Ph.D., D.V.M., nutrition and biochemistry. Research and teaching experience in university and laboratory. Seeking essentially research position. Prefer Southeast. Box 53, SCIENCE. X

Plant Pathologist-Mycologist desires teaching and/or research position. Ph.D., teaching and research experience; publications in several journals; minimum salary $9500. Box 58, SCIENCE. X

Research Administrator; Ph.D. (major, organic chemistry; minors, pharmacology and toxicology); broad experience as director of research and development. Medical Bureau, Burneice Larson, Director, 900 North Michigan Avenue, Chicago. X

Veterinarian, experienced in microbiological techniques, presently at a medical school, desires position as director of experimental animal laboratory. Box 54, SCIENCE. X

Virologist; Ph.D., 30. Tissue culture and vaccine research. Strong background in biochemistry and cell physiology. Publications. Academic or industrial. Box 46, SCIENCE. 3/13

POSITIONS OPEN

Anatomist with training and interests in pathology to head new section on comparative pathology in medical research institute. Opportunity for academic affiliation with restricted teaching responsibilities. Central states location. Box 49, SCIENCE. 3/13

POSITIONS OPEN

Anatomist. Instructor to teach gross anatomy one semester. Remainder of year for research. Position permanent. Initial salary $6000. Send curriculum vitae, photograph, and two references to Chairman, Department of Anatomy, University of Louisville School of Medicine, Louisville 2, Kentucky. 3/20

The University of Alberta invites applications for a position in the **Department of Animal Science as Assistant Professor.** The starting salary will be between $6000 and $7700 according to qualifications and experience; excellent prospects for advancement. Postgraduate education equivalent to the Ph.D. is required. Duties, to commence between 1 May and 1 September 1959, include research in fundamental and applied nutrition with dairy cattle, teaching, and limited extension work.

Applications, accompanied by a recent photograph and giving age, nationality, and other personal information; academic qualifications and experience; list of publications and names and addresses of three references, should be addressed to the Head, Department of Animal Science, University of Alberta, Edmonton, Alberta. Closing date: 15 April 1959. 2/27; 3/13

Assistant or Associate Professor to develop a curriculum in electrical engineering and eventually be chairman, in a private engineering school in northern California college. Send detailed résumé, references, recent photo, state salary to Box 39, SCIENCE. 2/27; 3/6, 13

Biochemist or Physiologist. Biochemist or physiologist with biochemical orientation to participate in studies on cardiovascular-renal physiology. Experience in tissue analysis and isotope techniques desirable. May Institute, 421 Ridgeway Avenue, Cincinnati 29, Ohio. 3/6, 4/3

(a) Medical Consultant qualified to promote effective projects including medical educational programs; would work closely with divisions throughout West; preferably someone with 5 years' practice; $12,000–$15,000. **(b) Instructor in Microbiology and Immunology;** duties consist of participating in teaching program for medical students and research; starting salary about $7000; Midwest. **(c) Ph.D.'s in Biochemistry and Pharmacology;** experience in proteins helpful but not essential; latter should be experienced in physiology and pharmacology; both candidates should possess administrative experience; starting salary $14,000. S3-2 Medical Bureau, Burneice Larson, Director, 900 North Michigan Avenue, Chicago. X

New World-Wide Graduate Award Directories for American scientists, teachers, librarians to subsidize their education and research. Stipends $200–$10,000. Volume I (1957), $3; volume II (just published, no duplication), $3; both volumes, $5. Limited editions. Complete, specific information on 400 awards in United States and overseas in each volume. CRUSADE, Sci., Box 99, Station G, Brooklyn 22, N.Y. eow

PHARMACEUTICAL CHEMIST

Tablet Research & Development

Young Ph.D.-level chemist, with 2 to 3 years' industrial experience in tablet research and development, to supervise tablet section in our Pharmaceutical Development Department.

In confidence send complete résumé and salary requirements to Personnel Director

SCHERING CORP.
60 Orange St. — Bloomfield, N. J.

Three Physical Science Positions. One Ph.D. with research and teaching experience to head Department of Physics, starting salary $10,000–$11,000 for 11 months. One teacher each in chemistry and physics, M.S. to Ph.D., salary dependent on qualifications. Start September 1959. H. W. Gould, Northern Illinois University, DeKalb, Illinois. X

POSITIONS OPEN

Physiologist, cellular and general, secondary interest botany or bacteriology, strong interest in undergraduate teaching. Teacher's and liberal arts college. New building under construction with good facilities teaching and research. Apply Chairman, Science Department, Western Washington College, Bellingham, Washington. X

Plant Pathologist; Ph.D. to be project leader of fungicides and nematocides laboratory whose primary function is screening and evaluating for new candidate pesticides. Biochemistry, fungus physiology, and/or plant physiology are desirable minor disciplines which aid the professional biologist in contributing to successful synthetic research program. Write Research Director, Niagara Chemical Division, Middleport, New York, for application for employment blank. X

Research and Teaching Assistantships in anatomy are available to qualified persons to study toward the Ph.D. degree. A background in biological sciences with some chemistry is desirable. Stipends begin at $2400 per year. Write Head of Anatomy Department, College of Medicine, University of Florida, Gainesville, Florida. 2/27; 3/6; 13

Research Assistant, B.S. or M.S. Conscientious person with good college record in chemistry and willingness to learn. Desired for work on the central nervous system employing biochemical and biophysical techniques. Salary consistent with training and experience. Midwestern university. Box 43, SCIENEC. 3/13, 20

SCIENCE TEACHERS, LIBRARIANS, ADMINISTRATORS urgently needed for positions in many states and foreign lands. Monthly non-fee placement journal since 1952 gives complete job data, salaries. Members' qualifications and vacancies listed free. 1 issue, $1.00. Yearly (12 issues) membership, $5.00. CRUSADE, SCI., Box 99, Station G, Brooklyn 22, N.Y. ew

UNIVERSITY OF ALBERTA
Faculty of Agriculture

Applications are invited for a position in the department of plant science as **Assistant Professor of Plant Pathology.** The starting salary will be between $6000 and $7000, depending on qualifications and experience, and there are excellent opportunities for advancement. Postgraduate education equivalent to the Ph.D. in plant pathology and related fields is required. The person appointed will be expected to assist in the teaching of plant pathology, in general plant pathological work, and in the development of a strong program of research. Excellent laboratory, field, and greenhouse research facilities are available.

Applications, accompanied by a recent photograph and giving age, nationality, and other personal information; academic qualifications and experience; list of publications and names and addresses of three references, should be submitted to the Head, Department of Plant Science, University of Alberta, Edmonton, Alberta, Canada. **Closing date: 1 May 1959.** 3/6, 13

FELLOWSHIPS

The Botany Department, University of Western Ontario invites applications for two posts (1) a National Research Council postdoctoral fellowship in pathology, mycology, physiology, or cytology. Annual stipend $3700–$4500. Tax free. Travel allowance. (2) A postgraduate fellowship for study of microorganisms involved in cellulose decomposition. Annual stipend $2500. Applications with curriculum vitae and names of two referees should be sent promptly to D. G. Wilson, Acting Head, Department of Botany, University of Western Ontario, London, Canada. 3/20

The Market Place

BOOKS • SERVICES • SUPPLIES • EQUIPMENT

DISPLAY: Rates listed below—no charge for Box number. Monthly invoices will be sent on a charge account basis — provided that satisfactory credit is established.

Single insertion	**$26.00 per inch**
13 times in 1 year	**24.00 per inch**
26 times in 1 year	**23.00 per inch**
52 times in 1 year	**22.00 per inch**

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

PROFESSIONAL SERVICES

USE THIS EASY SELF-MAILER to obtain further information

13 March 1959

Readers' Service

Information Requisition

It's simple: Mark—Clip—Fold—Mail—No stamp required

This coupon is for your convenience—to facilitate your requests for further information about advertised products and items in Equipment.

From:

Name ..... **Position** .....

Company .....

Street .....

City ..... **Zone** ..... **State** .....
(Please print or type)

Mark, clip coupon—FOLD HERE along this line—mail

Postage Will be Paid by Addressee

No Postage Stamp Necessary If Mailed in the United States

BUSINESS REPLY MAIL
First Class Permit #12711 New York, N.Y.

Readers' Service
To: SCIENCE MAGAZINE
Room 740
11 West 42 Street
New York 36, New York

Fasten Here Only
Staple, Tape, Glue

13 March 1959

Readers' Service

Information Requisition

Use this easy self-mailer to obtain further information about items or literature from the Equipment section as well as from advertised products.

EQUIPMENT

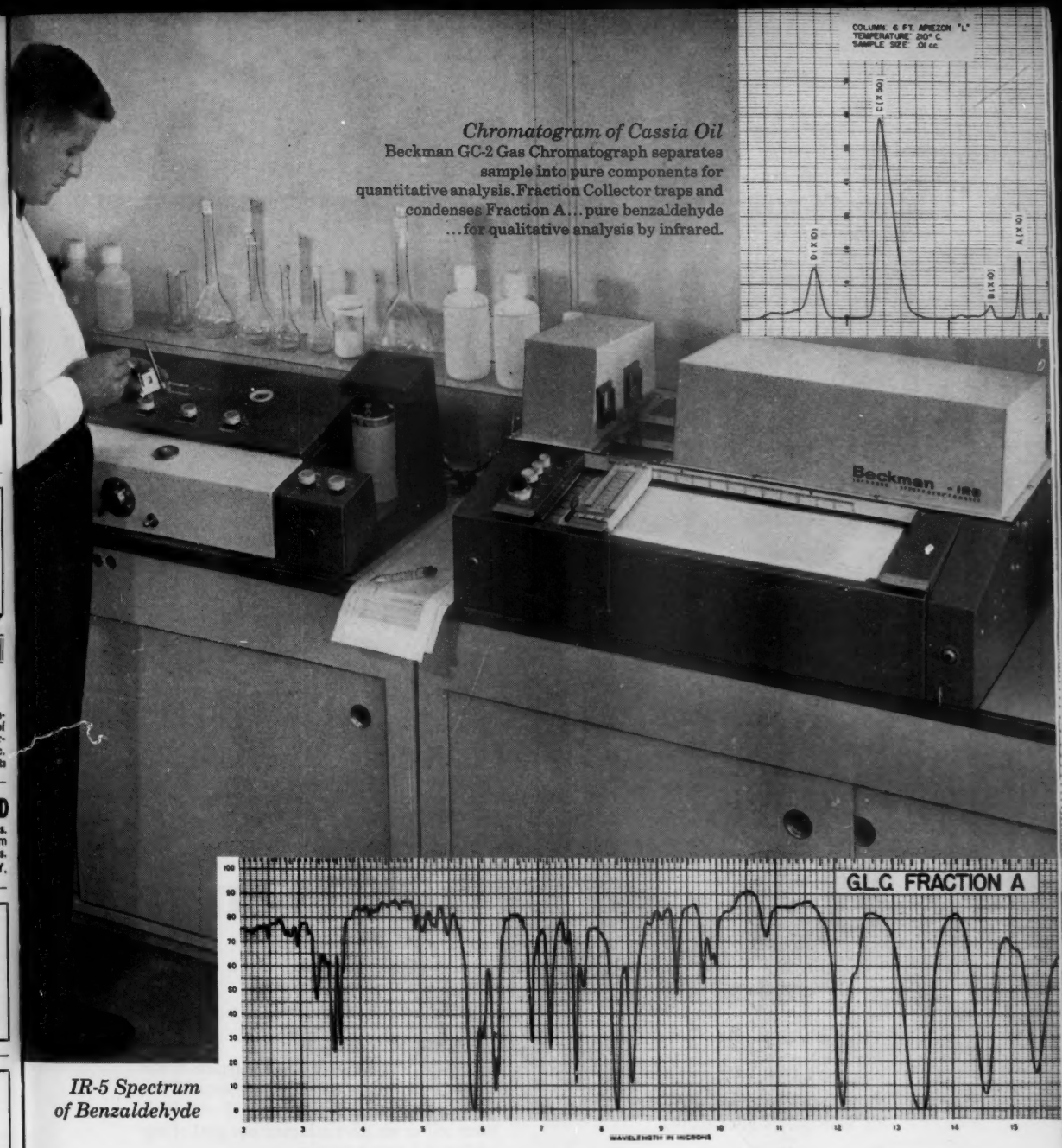
Circle below desired number corresponding to:

680 682 685 686 687 688 689 691
692 694 695

ADVERTISERS IN THIS ISSUE

In list below, check page number of advertiser from whom you would like more information. If more than one item appears in ad, letters (A, B, C) are used to indicate particular items available in order of appearnce in advertisement. Where more than one ad appears on page, **"U" indicates upper ad, "L" lower ad, "I" inside ad, "M" middle ad,** and **"O" Outside ad.** The covers are designated by **IFC** (inside front cover), **IBC** (inside back cover), and **OBC** (outside back cover). Advertisements in Personnel Placement and Market Place are not keyed. A multiplicity of items is indicated by *. Readers are requested to specify on this coupon the particular item in which they are interested; otherwise, the request cannot be processed.

☐ IFC	☐ 683*	☐ 684, A	☐ 684, B	☐ 688
☐ 724	☐ 725, UI	☐ 725, UO*	☐ 725, LO	☐ 726, A
☐ 726, B	☐ 727, I-A	☐ 727, I-B	☐ 727, I-C	☐ 727, O
☐ 728, UO*	☐ 728, UI	☐ 728, LO	☐ 728, LI	☐ 729
☐ 730, A	☐ 730, B	☐ 730, C	☐ 731, U	☐ 731, LM
☐ 731, LO*	☐ 732, LO	☐ IBC	☐ OBC	



Chromatogram of Cassia Oil
Beckman GC-2 Gas Chromatograph separates sample into pure components for quantitative analysis. Fraction Collector traps and condenses Fraction A... pure benzaldehyde ...for qualitative analysis by infrared.

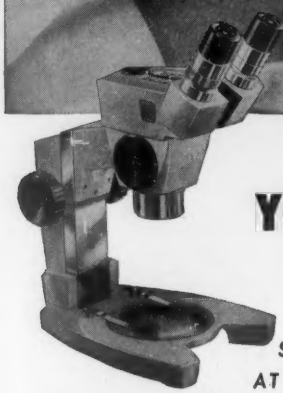
IR-5 Spectrum of Benzaldehyde

What's missing in this Infrared Spectrum of Benzaldehyde? Benzoic acid impurities, of course! Pure benzaldehyde has always been difficult to prepare and even more difficult to analyze before it decomposes. But now, this problem can be solved by combining a GC-2 Gas Chromatograph and an IR-5 Infrared Spectrophotometer into one analytical system. The GC-2, with Fraction Collector, isolates the pure fraction which is then transferred to an IR-5 microcell for analysis. In just sixteen minutes the IR-5 produces this complete 2-16 micron spectrum of benzaldehyde. ⌘ These Beckman instruments allow complete separation and positive identification of samples as small as 0.0002 cc...both quantitative and qualitative analyses of organic mixtures...with speed and accuracy. To learn more about the high-temperature GC-2 and double-beam IR-5, write for Data File 2L-52-38.

Beckman
Scientific and Process Instruments Division
Beckman Instruments, Inc.
2500 Fullerton Road, Fullerton, California

It's a Fact: **Beckman portable oxygen analyzers used with hospital incubators help prevent Retrolental Fibroplasia, a disease of premature infants which is caused by excess oxygen and can lead to partial or complete blindness.**

Multi-exposure shot showing "PERMANENT" mounted prism being crashed into a piece of wood. Bond was not affected in any way. Your AO Sales Representative will perform this demonstration right before your eyes.



YOU CAN PAY MORE BUT YOU CAN'T BUY BETTER

AMERICAN-MADE AO SPENCER CYCLOPTIC STEREOSCOPIC MICROSCOPES START AT A LOW $202.50* . . .

This stroboscopic photograph shows the amazing holding power of the specially developed "PERMANENT" bonding agent used to mount prisms in the new AO Spencer Cycloptic Stereoscopic Microscopes.

This method of prism mounting means you can put your Cycloptic to extreme use...attachment to a vibrating production machine, rough and tumble field trips, even years of student handling...and still be assured of positive, permanent prism alignment.

This careful attention to detail is typical of the thoroughness that marked every step of the development of this instrument. Enthusiastic users tell us we have achieved our goal of top quality at a low, low cost.

The entire AO Spencer Stereoscopic story is yours for the asking. Mail coupon below for handsome 36 page brochure which gives complete specifications.

***Model 56F-1, in quantities of 5 or more**

AO SPENCER

American Optical Company

INSTRUMENT DIVISION BUFFALO 15, NEW YORK

Dept. O-2

Gentlemen:

Please send me AO Spencer Cycloptic Brochure SB56-856.

Name_____

Address_____

City_____ Zone____ State_____